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THE AMERICAN HEART JOURNAL

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The American Heart Journal

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The American Heart Journal

VOL. III DECEMBER, 1927 No. 2

Original Communications

EXTREME DILATATION OF THE LEFT AURICLE TO THE RIGHT*

D. EVAN BEDFORD, M.D., M.R.C.P.
LONDON, ENG.

THE clinical and anatomical features of extreme enlargement of the left auricle to the right were first described in 1901, by Sir Isambard Owen and W. J. Fenton.[1] In their patient, a woman aged forty years, with mitral stenosis and an irregular pulse, there was systolic pulsation and thrill in the right axilla, and dullness at the right lung base suggesting pleural effusion. Paracentesis was performed via the sixth space in the right midaxillary line, but instead of serous fluid, blood was withdrawn. Necropsy revealed enormous dilatation of the left auricle, which projected beyond the right auricle almost to the chest wall. The capacity of the dilated auricle was 30 ounces.

Since their description, further similar cases have been reported from time to time so that the anatomy, clinical associations, and physical signs are now better known. Even in its earliest stages, before obvious physical signs appear, projection of the left auricle to the right is demonstrable with certainty by x-ray examination. It is owing to the perfection of technic in radioscopic methods of examination of the heart attained in France and Germany that this condition has received wider recognition in those countries than in England or America. Bordet,[2] in a large series of cases of mitral stenosis examined by x-ray methods, found extension of the left auricle to the right, beyond the right auricle, in 5 per cent.

CASE REPORTS

The following two cases, at present under my observation, exemplify an extreme grade of this condition.

*From the Cardiographic Department of the London Hospital, and the National Hospital for Diseases of the Heart, London.

CASE 1.—Female, aged twenty-one years, was seen at the National Hospital for Diseases of the Heart in March, 1926. She complained of winter cough, palpitation and irregular beating of the heart, breathlessness on exertion, and exhaustion. Sometimes swallowing was difficult; the food seemed to stick so that she had to bring it back.

History.—Tonsillitis several times. "Growing pains" in the ankles in childhood, but no definite history of acute rheumatism or chorea. She had suffered from "thumping" of the heart for many years. At seven years of age a doctor had found heart trouble. Aged fourteen, she was in hospital with heart failure but recovered, and since this she had kept fairly well.

Examination.—She was of slender build and undersized. There was slight cyanosis, but no dyspnea when at rest. Pulse was completely irregular, rate 70. There was bulging of the precordia and diffuse heaving cardiac pulsation. Broadbent's sign was present. Apex beat in the sixth interspace in the anterior axillary line. Apical diastolic thrill. Systolic and rumbling diastolic murmurs were heard at the apex, and a systolic and faint diastolic murmur at the aortic area. In the right axilla forcible systolic pulsation was palpable, maximal in the fourth and fifth interspaces in the midaxillary line. There was a definite systolic thrill in the right axilla. On auscultation over this area of pulsation a systolic murmur was heard, louder than at the apex. On percussion there was dullness to the right of the sternum, the upper limit extending from the second sternocostal junction obliquely

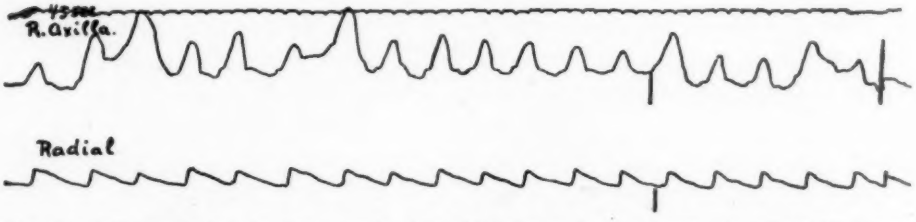


Fig. 1.—The pulsation in the fourth right interspace in the axilla is recorded above, and the radial pulse below. The pulsation is systolic in time.

downwards to the fifth space in the right midaxilla. There was some impairment of note over the whole right axilla on firm percussion, and over the lower lobe of the right lung posteriorly. The breath sounds at the right lung base were diminished.

There were no signs of congestive failure; the jugular veins were not engorged nor did they pulsate noticeably. Fig. 1 shows a simultaneous record of the axillary pulsation, in the right fourth intercostal space, and of the radial pulse; the axillary pulsation is systolic in time. The electrocardiogram showed auricular fibrillation and right ventricular predominance. In the absence of right-sided engorgement and of all evidence of tricuspid regurgitation, the presence of forcible systolic pulsation and of a systolic thrill and murmur in the right axilla could only be explained by great enlargement of the left auricle with mitral regurgitation.

X-ray examination.—The radiogram is seen in Fig. 2. The heart was slightly enlarged to the left, and the pulmonary artery was prominent. On the right side, the heart shadow extended to the chest wall; at the lower half of the right border there was a definite localized bulge to the right. On screen examination expansile systolic pulsation of the right border was visible. The vascular pedicle was narrow and there was no dilatation of the superior vena cava. After swallowing barium paste, the esophagus was seen to be displaced to the right at the upper level of the auricle, and there was delay at this point. In the first oblique position (patient facing half left) the barium was seen to be held up above the auricle, which projected backwards into the retrocardiac space; a thin stream of barium trickled

round the convex border of the auricle. The orthodiagram is seen in Fig. 3; the total transverse diameter of the heart was 19.1 cm., midline to left border 8.4 cm., midline to right border 10.7 cm.

CASE 2.—A woman aged thirty-five years was seen at the National Hospital for Diseases of the Heart in March, 1926. She complained of breathlessness, and a sharp pain in the right side of the chest on exertion which was relieved by resting.

History.—No acute rheumatism or chorea. She had been well until 1914 when she had hemoptysis following influenza. Six months later a further hemoptysis

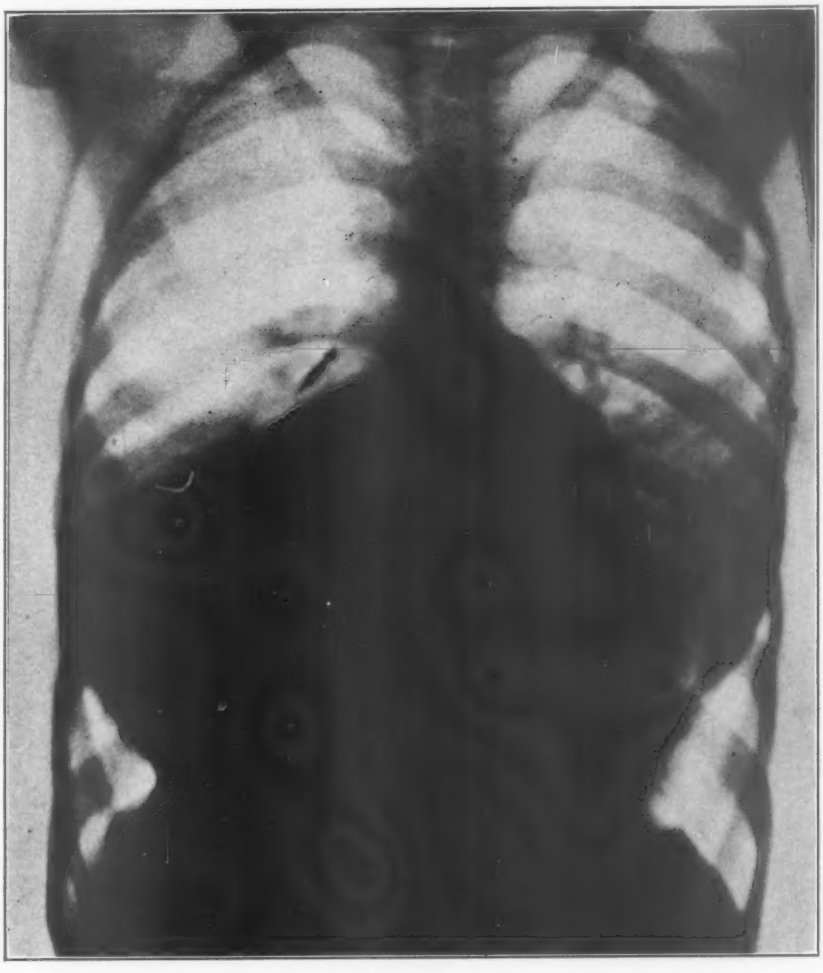


Fig. 2.—Radiogram from Case 1. The dilated left auricle extends to the right chest wall.

occurred, and heart disease was diagnosed. Since 1914 she had been easily breathless, but otherwise fairly well.

Examination.—She was slightly cyanosed, but not breathless while at rest. Pulse was completely irregular. Apex beat was forcible, in the sixth interspace external to the midclavicular line. There was a purring apical diastolic thrill. On auscultation at the apex there was heard an accentuated first sound, a systolic murmur, a reduplicated second sound, and a diastolic murmur. A faint aortic diastolic murmur was audible along the left sternal border. There was periapical systolic retraction and a well-marked Broadbent's sign.

In the anterior part of the right axilla forcible systolic pulsation was palpable, maximal in the fifth interspace. On auscultation over the pulsation in the right axilla the first sound and a systolic murmur were heard almost as clearly as at the apex. There was dullness to the right of the sternum in the third and fourth interspaces, extending an inch and a half from the sternum at the cardiohepatic angle, and slight impairment of percussion note in the right axilla and at the right lung base. The breath sounds at the right base were diminished.

There were no signs of congestive heart failure; the neck veins were not engorged nor did they pulsate abnormally. The liver was not enlarged. The electrocardiogram showed auricular fibrillation and right ventricular predominance. For the same reasons as in the previous case the pulsation in the right axilla was explainable only by supposing enlargement of the left auricle to the right.

X-ray examination.—The radiogram is seen in Fig. 4. The enlargement to the right is characteristic, but less than in the previous case. The maximum projection to the right is well above the diaphragm level, and the cardiohepatic angle is acute. A convex bulge of the left auricle at the middle of the right heart border is well

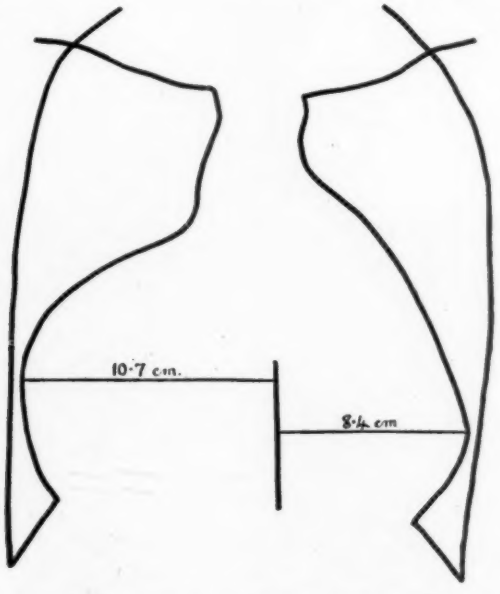


Fig. 3.—Orthodiagram from Case 1. The total transverse diameter is 19.1 cm.

seen, and in the upper part the right border of the right auricle can be distinguished through it. The esophagus was not displaced laterally, but in the oblique view there was delay at the upper border of the auricle and displacement backwards.

PATHOLOGY

In almost all reported cases, extreme dilatation of the left auricle to the right has been associated with mitral stenosis and often with adherent pericardium; the latter is presumptive evidence of severe rheumatic carditis. The auricular wall has usually shown evidence of old inflammatory change and been the site of pericardial adhesions. The wall is thinned, translucent, and fibrous, with little or no muscular tissue remaining. In Batty Shaw's case[3] the auricle held 30 ounces, in Emanuel's case,[4] 40 ounces. Two factors seem responsible

for this extreme dilatation of the auricle: myocarditis of the auricular wall, and increased intraauricular pressure from mitral stenosis and presumably mitral regurgitation. Where the fibrous pericardium is involved in a rheumatic inflammatory process the normal support of the auricles must be diminished. In East's case[5] the wall of the left auricle consisted of a very thin band of muscle mixed with fibrous

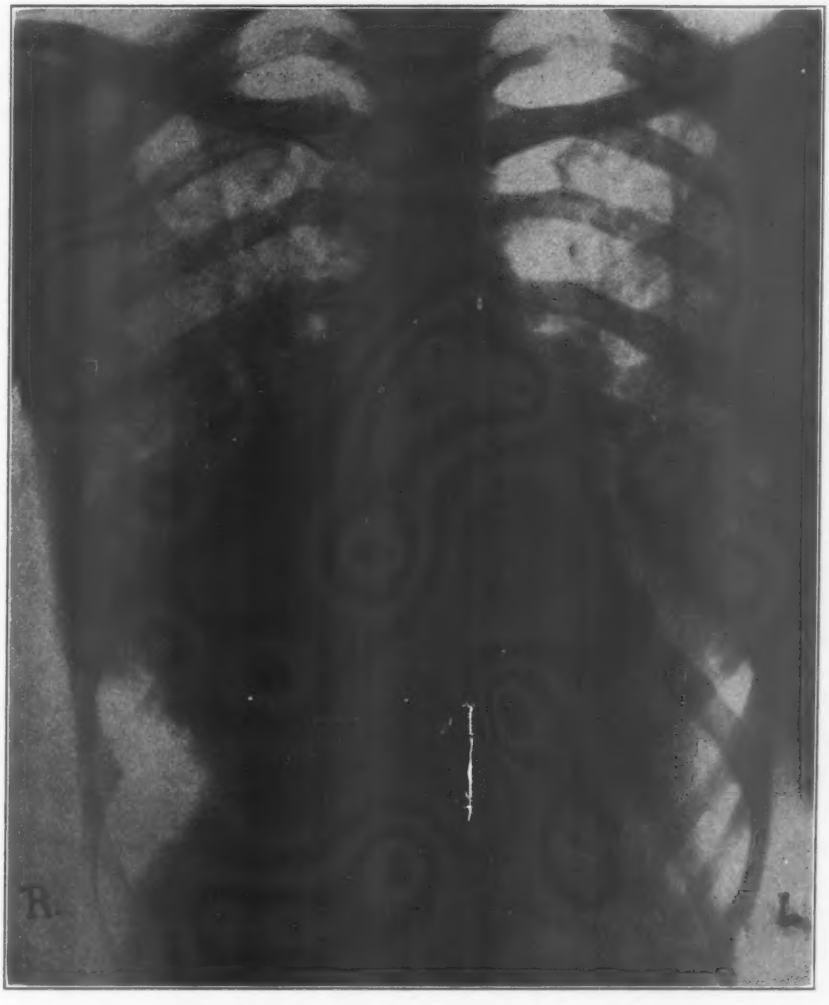


Fig. 4.—Radiogram from Case 2. The convex bulge of the left auricle to the right is seen just below the right lung root, which is increased in density.

tissue, and dense fibrous tissue on the pericardial side. Other cases of dilatation of the left auricle to the right associated with mitral stenosis have been recorded by Assmann,[6] Rösler and Weiss,[7] Rosselet and Bach,[8] Lutembacher,[10] and Bordet.[2] The pathology in Lutembacher's cases was interesting. In one, with a rheumatic mitral lesion and infective endocarditis, numerous small infarctions were found on the posterior surface of the left auricle; an aneurysmal bulge to the right

occurred at the site of a sharply demarcated fibrous scar, the result of old infarction. In the second case, without a valvular lesion, there was also an aneurysmal bulge of a fibrous scar in the wall of the auricle. In a third case,[9] with mitral stenosis, there was an aneurysmal pouch of the left auricle projecting to the right at the site of a tuberculous abscess of the lung.

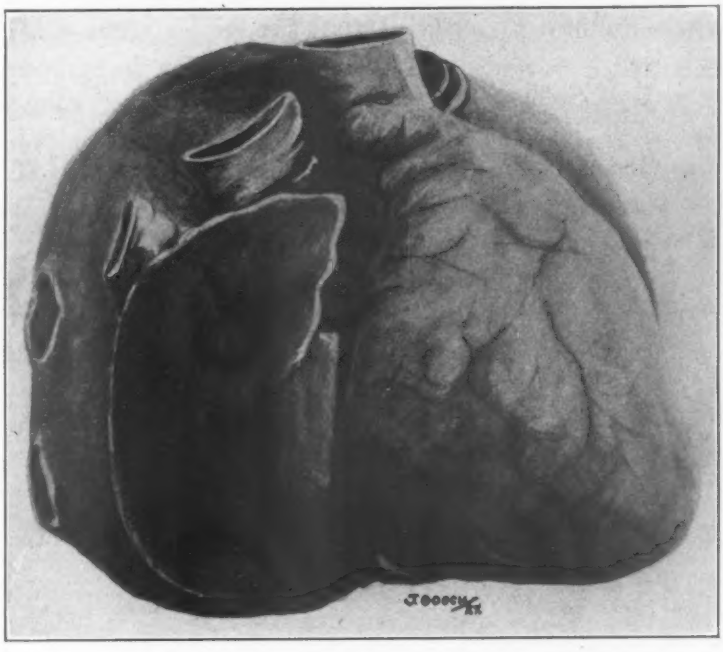
ANATOMY

The anatomical relations of the heart chambers in this condition are seen in the drawing in Fig. 5, from a specimen in the Pathological Institute of the London Hospital. The patient was a woman aged thirty-three, who died in the hospital from pulmonary embolism. There was fibrotic thickening, slight calcification, and fusion of the stenosed mitral valve, recent rheumatic vegetations on the contact margins of two posterior cusps of the aortic valve, and chronic inflammatory thickening of the free margins of the tricuspid valve. Seen from the front the left auricle extended to the right of the right auricle and above it. The left auricular appendix was almost completely absorbed into the main cavity of the auricle, so that there was no projection of the left auricle in this region. The right auricle was displaced forward and slightly to the right, lying entirely in front of the left auricle. The interauricular septum was placed almost in a coronal plane. An additional feature of interest in this specimen was an aneurysmal protrusion of the left auricle through the fossa ovalis into the right auricle. Seen from the interior of the right auricle (Fig. 6) this appeared as a tongue-shaped projection 3 cm. in length; its wall was translucent and as thin as tissue paper. The cavity of the left auricle contained a ball thrombus measuring 2.5 cm. in diameter.

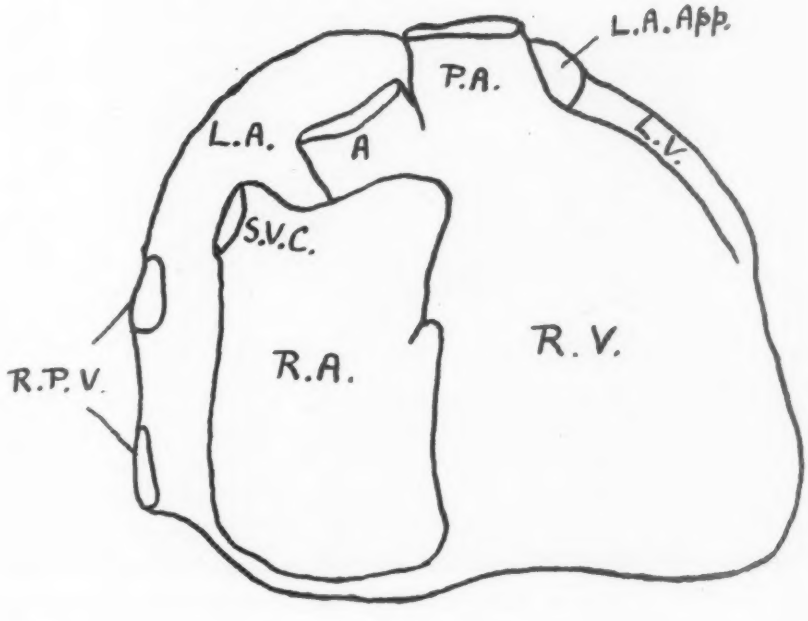
The effect of extreme enlargement of the left auricle on surrounding organs has been carefully studied by Kovács and Stoerk,[11] and by Gäbert.[12] Pressure on the tracheal bifurcation from below makes the angle between the main bronchi more obtuse than normal. Displacement of the esophagus is important as it can be so readily demonstrated during life by radioscopic examination. Usually the esophagus is displaced to the right at the upper border of the auricle; it then curves backward round the wall of the auricle and forward again to the cardia. There must be some degree of compression of the esophagus, and this can be demonstrated by x-ray examination.

SYMPTOMS AND PHYSICAL SIGNS

Apart from the usual symptoms associated with mitral stenosis and adherent pericardium, certain special symptoms may arise. There may be pain on swallowing or some difficulty in swallowing, as in Case 1. Pain in the chest is common and may be felt in the right



A.



B.

Fig. 5.—Drawing of specimen seen from the front. The dilated left auricle forms the whole right border of the heart. *R.A.*, right auricle; *L.A.*, left auricle; *R.V.*, right ventricle; *L.V.*, left ventricle; *L.A. App.*, left auricular appendix; *P.A.*, pulmonary artery; *A.*, aorta; *S.V.C.*, superior vena cava; *R.P.V.*, right pulmonary veins.

axilla, under the right breast, or at the right lung base. In Case 2 the pain was induced by exertion and was always relieved by resting. Dry cough was troublesome in one case and may have been due to pressure on the tracheal bifurcation, as there was no congestion of the lungs.

In the earlier stages there are no characteristic physical signs, and the diagnosis is only possible by radioscopic examination. When the left auricle approaches the right chest wall, however, the signs are suggestive. There is a variable area of dullness to the right of the sternum and in the right axilla. Forcible systolic pulsation is palpable to the right of the sternum and in the right axilla at the level of

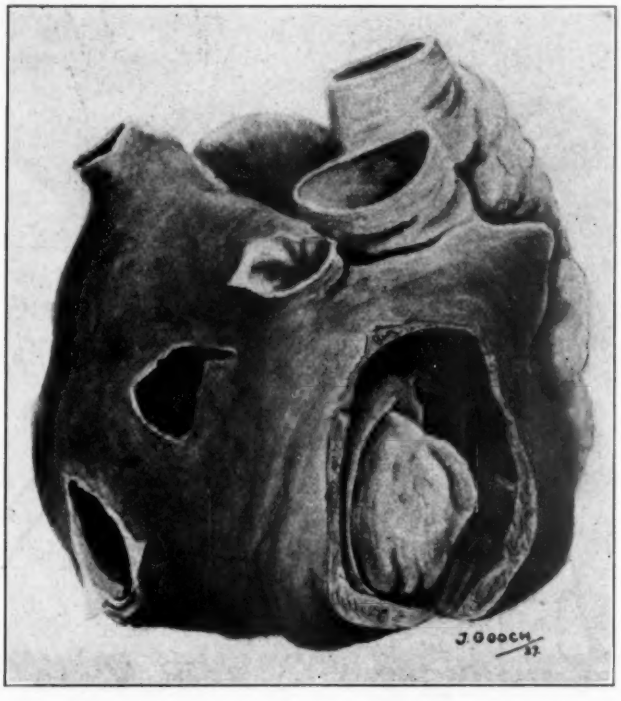


Fig. 6.—The same heart as in Fig. 5, seen from the right side. The dilated left auricle and orifices of the right pulmonary veins are seen on the left. The anterior wall of the right auricle has been partly removed to show the aneurysmal bulge of the left auricle through the fossa ovalis into the right auricle.

the fourth or fifth interspace, due to regurgitation through the mitral valve. In almost all recorded cases auricular fibrillation has been present, and therefore presystolic pulsation is not to be expected, though it seems doubtful whether the thin fibrous sac which constitutes the auricle in these cases could in any case cause a perceptible impulse by itself. There may be a systolic thrill in the right axilla as in Case 1, and as in Emanuel's case. The heart sounds are audible over the area of pulsation in the right axilla and the systolic murmur is louder there than at the apex. In all cases that I have seen there has been diminished air entry and some degree of dullness on percus-

sion at the right lung base posteriorly. These signs may suggest pleural effusion, and in two recorded instances the left auricle was actually punctured during attempted paracentesis. In both the present cases and in others that I have seen congestive heart failure was absent. When there is no engorgement or noticeable pulsation of the

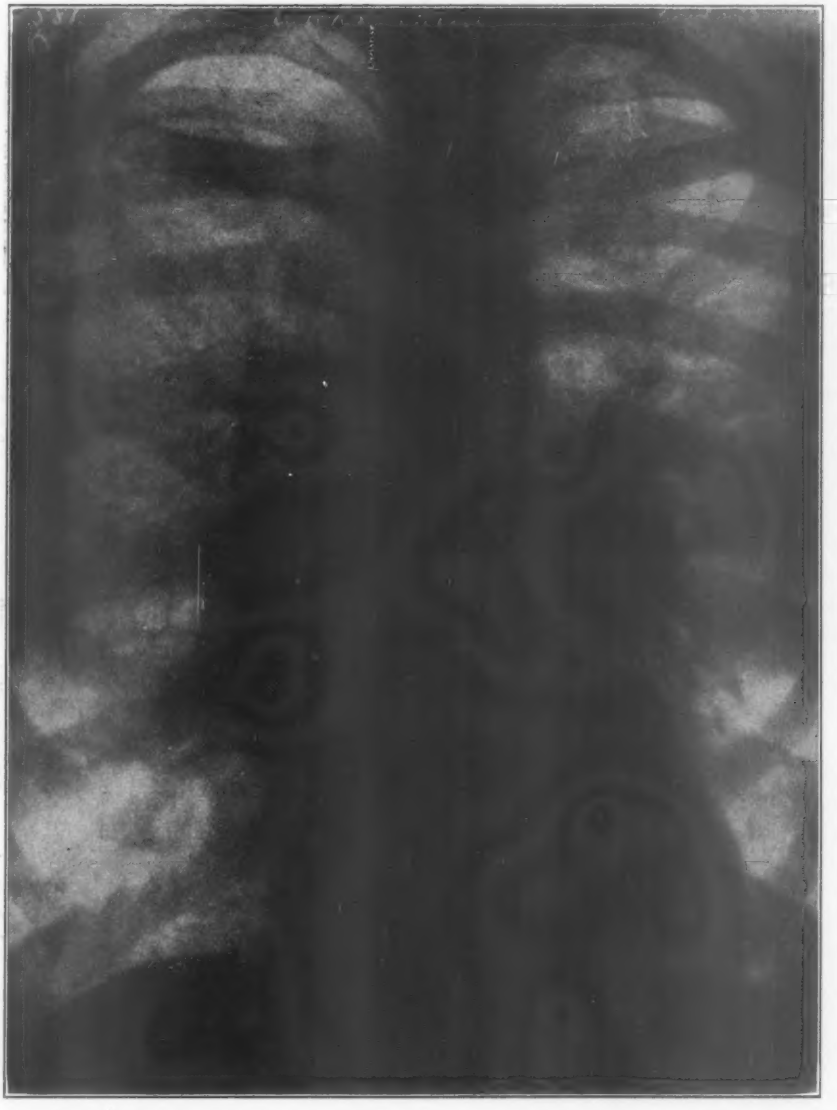


Fig. 7.—Radiogram from a case of mitral stenosis showing an early stage of enlargement of the left auricle to the right. The left auricle forms a small knob-like projection in the middle of the right heart border, below the right lung root.

jugular veins and no liver pulsation the exclusion of tricuspid regurgitation and extreme dilatation of the right auricle is easy. It is doubtful whether or not the right auricle ever causes pulsation in the right axilla. Dullness to the right of the sternum may suggest

pericardial effusion, but this should be excluded when there is forcible pulsation and a loud murmur or thrill over the dull area.

X-RAY DIAGNOSIS

In the frontal view the projecting left auricle forms part or the whole of the right border of the cardiac shadow, and produces a

Fig. 8.—Oblique radiogram from same Case as Fig. 7, showing the typical appearance of the left auricle projecting into the postcardiac space well above the diaphragm level.

sharply convex bulge to the right; the maximum projection to the right is usually some inches above the diaphragm level, and the cardiohepatic angle is thus acute. In extreme degrees of enlargement the left auricle may form the whole right border of the heart outline.

In enlargement of lesser degree the left auricle projects to the right above the right auricle which forms the lower part of the right border of the cardiac shadow. The radiogram in Fig. 7 exemplifies this early stage. The patient was a male, aged twenty-one years, with signs of mitral stenosis and adherent pericardium.

Screen examination shows vigorous systolic pulsation of the left auricle from mitral reflux, making the distinction from pericardial effusion easy. Displacement of the esophagus to the right at the upper level of the auricle can be demonstrated by means of barium paste.

In the case of great enlargement of the right auricle the maximum projection to the right is usually at or near the diaphragm level; the right border of the heart is flattened, and the cardiohepatic angle is more obtuse. Furthermore, dilatation of the superior vena cava causes widening of the vascular pedicle.

In either of the anterior oblique positions, at about 60 degrees, the left auricle is seen projecting backward into the postcardiac space, sometimes an inch or more above diaphragm level (see Fig. 8). By means of barium paste the compression and deviation backward and laterally of the esophagus can be easily made out in this position. Usually the barium is delayed at the upper level of the auricle, where the esophagus may be slightly dilated, and trickles slowly, in a thin stream, round the convexity of the auricle.

I am indebted to Dr. John Parkinson for permission to publish the two cases described, and to Dr. F. G. Nicholas for the radiograms in Figs. 7 and 8. Professor H. M. Turnbull kindly allowed me to describe the specimen from the Pathological Institute of the London Hospital, shown in Figs. 5 and 6.

SUMMARY

Two cases of extreme dilatation of the left auricle toward the right are described. The symptoms, physical signs, and diagnosis are discussed, and the x-ray appearances are described in detail. Deviation of the esophagus to the right at the upper level of the dilated auricle is characteristic. In the early stages diagnosis is possible only by means of x-ray examination, but in the later stages suggestive signs and symptoms may appear. The condition is almost always met with in association with mitral stenosis and auricular fibrillation, and usually with adherent pericardium. A pathological specimen exemplifying the condition is described and portrayed.

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A STUDY OF THE COURSE OF RHEUMATIC HEART DISEASE*

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THE marked increase in heart disease in this country during the last twenty years has been forcibly brought to the attention of the profession by Cohn and others.[1, 2, 4] Cohn recently has shown how the death rate from pulmonary tuberculosis has fallen, how the death rate from pneumonia has not equalled that of heart disease since 1910, and how the rate from cancer is mounting, but even now is relatively low as compared to that of heart disease. Rheumatic fever is one of the most important etiological factors.

The present study is limited to a consideration of the course of rheumatic heart disease. One hundred sixty cases of rheumatic heart disease have been studied in which data were available from the time of the initial infection until death occurred from heart disease. Only those cases were included in which a structural valvular lesion typical of rheumatic heart disease was presented with a definite history of one or more attacks of rheumatic fever characterized by febrile illness with migratory involvement of the larger joints. In six cases history of joint involvement was not obtained, but clear-cut histories of chorea were.

AGE AND SEX

The age of the patient at the time of examination in the Mayo Clinic will be first considered. In 81 per cent of the cases the age was less than fifty. The greatest incidence occurred in the fifth, fourth, and third decades in which forty-seven cases (29 per cent), thirty-eight cases (24 per cent), and thirty cases (19 per cent) occurred respectively. The number of cases in which the age is more than fifty years diminishes rapidly, the incidence for the three decades being only seventeen cases (19 per cent). In the complete group the incidence for the two sexes was equal, eighty of each. There was a fairly uniform distribution according to age groups (Table I).

TABLE I

AGE AND SEX INCIDENCE AT THE TIME OF EXAMINATION (COMPLETE GROUP)

DECADE	CASES		SEX	
	NUMBER	PER CENT	MALES	FEMALES
0- 9				
10-19	14	9	5	9
20-29	30	19	15	15
30-39	38	24	20	18
40-49	47	29	21	26
50-59	22	14	11	11
60-69	7	4	6	1
70-79	2	1	2	
Total	160	100	80	80

*Section on Cardiology, Mayo Clinic.

The following data throw some light on the duration of rheumatic heart disease. The age and sex incidences of the same group are considered at the time of the first attack of rheumatic fever. It is necessary to assume that injury to the heart occurred at the time of the initial attack of rheumatic fever, although in some instances in this study this assumption may introduce an error.

It is interesting to note that the first attack of rheumatic infection occurred before the age of thirty in 136 cases (85 per cent) and before the age of twenty in 103 cases (64 per cent). The greatest incidence was in the second decade of life in which seventy-four cases (46 per cent) were recorded. In only five cases (3 per cent) did the primary infection occur after the fortieth year (Table II).

The average age at the time of death was thirty-two years. Patients who had attacks of rheumatic fever in the first decade of life attained an average age of thirty-one years, those in the second decade an average of thirty-eight years (Table II).

The time elapsing from the first attack of rheumatic infection to cardiac death was much shorter in the case of elderly patients than in young patients (Table II). Patients in the fifth and sixth decades

TABLE II

AGE AT TIME OF FIRST ATTACK OF RHEUMATIC FEVER AND DURATION OF THE DISEASE ACCORDING TO SEX (COMPLETE GROUP)

DECADE	AVERAGE ATTACKS OF RHEUMATIC FEVER	CASES	PER CENT	SEX		AVERAGE AGE AT DEATH, YEARS	YEARS FROM FIRST ATTACK OF RHEUMATIC FEVER TO DEATH (AVERAGE)
				MALE	FEMALE		
0- 9	3	29*	18	10	19	31	25
10-19	2	74†	46	42	32	38	23
20-29	1	33‡	21	18	15	42	17
30-39	1	19	12	6	13	52	15
40-49	1	3	2	3		55	10
50-59	1	2	1	1	1	63	11
Total and average	2	160	100	80	80	32	14

*Two cases with history of chorea.
†Three cases with history of chorea.
‡One case with history of chorea.

TABLE III

MALES IN COMPLETE GROUP

DECADE	AVERAGE ATTACKS OF RHEUMATIC FEVER	CASES		AVERAGE AGE AT DEATH, YEARS	YEARS FROM FIRST ATTACK OF RHEUMATIC FEVER TO DEATH (AVERAGE)
		NUMBER	PER CENT		
0- 9	2	10	12	33	26
10-19	2	42	52	39	23
20-29	1	18	23	43	18
30-39	1	6	8	56	22
40-49	1	3	4	55	10
50-59	1	1	1	64	13
Total and average	1	80	100	41	22

lived only ten and eleven years following the first rheumatic infection, death occurring at an age considerably less than the average life expectancy. Patients in the first and second decades lived twenty-five and twenty-three years after the time of the initial infection.

A comparison of the sex ratios of the complete group may be noted in Tables III and IV. No striking differences are apparent with the exception that the age at death in males is slightly greater, forty-one years as compared to thirty-eight in females.

CLINICAL GROUPS

To permit comparative study the material is divided into three groups according to the clinical diagnosis of valvular involvement: (1) mitral, 124 cases, (2) aortic, twenty-one cases, and (3) combined mitral and aortic, fifteen cases.

In Group I clinical evidence of mitral stenosis was obtained in all the cases. In Group II there were six cases with clinical evidence of aortic insufficiency, three of aortic stenosis and twelve with evidence of aortic stenosis and insufficiency. Group III is composed of cases in which there was mitral stenosis associated with aortic stenosis in five cases, aortic insufficiency in two, and aortic stenosis and insufficiency in eight.

TABLE IV

FEMALES IN COMPLETE GROUP

DECADE	AVERAGE ATTACKS OF RHEUMATIC FEVER	CASES		AVERAGE AGE AT DEATH, YEARS	YEARS FROM FIRST ATTACK OF RHEUMATIC FEVER TO DEATH (AVERAGE)
		NUMBER	PER CENT		
0- 9	3	19	24	30	24
10-19	2	32	40	36	22
20-29	1	15	19	40	16
30-39	1	13	16	46	11
50-59	1	1	1	62	10
Total and average	2	80	100	38	17

TABLE V

GROUP WITH MITRAL INVOLVEMENT

DECADE	AVERAGE ATTACKS OF RHEUMATIC FEVER	CASES		SEX		AVERAGE AGE AT DEATH, YEARS	YEARS FROM FIRST ATTACK OF RHEUMATIC FEVER TO DEATH (AVERAGE)
		NUMBER	PER CENT	MALES	FEMALES		
0- 9	2	22*	18	5	17	33	26
10-19	2	59*	47	29	30	42	22
20-29	1	25*	20	11	14	42	18
30-39	1	15	12	4	11	49	16
40-49	1	2	2	2		57	13
50-59	1	1	1		1	62	10
Total and average	2	124	100	51	73	30	12

*One case with history of chorea.

TABLE VI

GROUP WITH AORTIC INVOLVEMENT

DECADE	AVERAGE ATTACKS OF RHEUMATIC FEVER	CASES		SEX		AVERAGE AGE AT DEATH, YEARS	YEARS FROM FIRST ATTACK OF RHEUMATIC FEVER TO DEATH (AVERAGE)
		NUMBER	PER CENT	MALES	FEMALES		
0- 9	1	2*	10	1	1	43	36
10-19	1	8	38	8		42	27
20-29	1	7	33	7		41	16
30-39	1	3	14	2	1	49	13
50-59	1	1	5	1		64	13
Total and average	1	21	100	19	2	43	22

*One case with history of chorea.

Group I (Involvement of Mitral Valves).—This group is comprised of 124 cases, and shows a definite dominance of females, fifty-one members of the group being males and seventy-three females, a ratio of 2:3 (Table V). The initial attack of rheumatic fever occurred before the thirtieth year in 106 cases (85 per cent). This is the same proportion in which it occurred in the complete group. The greatest incidence was noted in the second decade—fifty-nine cases (47 per cent). Only three patients (3 per cent) were attacked by rheumatic infection for the first time after the fortieth year. The average age at which death occurred was thirty years, quite comparable to that in the complete series. The other data contained in Table V were also comparable to that in the complete group.

Group II (Involvement of Aortic Valves).—Twenty-one cases are recorded in this group. A striking disproportion in the sexes exists as there are nineteen males and two females, a ratio of 10:1 (Table VI). In this group, as in the others, marked preponderance of rheumatic infection occurred before the thirtieth year, seventeen cases (81 per cent). Initial infection was most frequent in the second and third decades where eight cases (38 per cent) and seven cases (33 per cent) are recorded. The average age at which death occurred in this group is forty-three years, definitely greater than in either the com-

TABLE VII

GROUP WITH BOTH MITRAL AND AORTIC INVOLVEMENT

DECADE	AVERAGE ATTACKS OF RHEUMATIC FEVER	CASES		SEX		AVERAGE AGE AT DEATH, YEARS	YEARS FROM FIRST ATTACK OF RHEUMATIC FEVER TO DEATH (AVERAGE)
		NUMBER	PER CENT	MALES	FEMALES		
0- 9	4	5	33	4	1	24	16
10-19	1	7	46	5	2	34	19
20-29	1	1	7		1	29	6
30-39	1	1	7		1	49	10
40-49	1	1	7	1		49	5
Total and average	2	15	100	10	5	32	16

plete group or in Group I. This observation is of interest but requires confirmation in a larger series of cases.

Group III (Involvement of Mitral and Aortic Valves).—Fifteen cases comprise this group. There is a striking dominance among males, ten cases as compared with five in females, a ratio of 2:1 (Table VII). In my experience, aortic involvement has been more prevalent among males, and the observation is borne out by the data in this study. There is again a marked preponderance of initial rheumatic infection before the thirtieth year, thirteen cases (86 per cent). Only two cases (14 per cent) occurred after that age. The average age at which death occurred was thirty-two years, almost identical to that in Group I.

RECURRENT RHEUMATIC INFECTIONS

In the complete group, recurrent rheumatic infections occurred most frequently in the first decade of life, sixteen cases (55 per cent). In one case eight distinct attacks of rheumatic fever occurred during a period of seven years. The average number of attacks for this age group was three (Table II). It is interesting to observe the progressive diminution in the number of recurrent attacks of rheumatic fever in the advancing decades. There were recurrent attacks in twenty-three cases (31 per cent) in the second decade, and the average number of attacks was two. In one case six attacks occurred within thirty-three years. There were only five cases (15 per cent) in which recurrent infection occurred in the third decade and the average number of attacks was only one for the group. In one case there were six recurrences within thirty-eight years. There was no instance of recurrent infection after the thirtieth year. Only one instance (5 per cent) of recurrent rheumatic infection occurred in Group II.

No constant relationship is revealed in this study between the number of attacks of rheumatic fever and the age at which death occurred. The average age at death of patients who had had one attack of rheumatic fever was forty years, while it was forty-eight years among those who had had six attacks (Table VIII). Undoubtedly the severity and extent of the primary cardiac injury and the rigidity of the instituted cardiac regimen are the important factors in determining the patient's expectation of life. Likewise, there is little difference between the incidence of recurrent infection in the two sexes (Table IX). The patients in this study were not related by blood and there are no reliable data regarding other members of the families. St. Lawrence[3] has called attention to the fact that there were multiple cases in the families that he studied.

ASSOCIATED DATA

Sixty-two patients (39 per cent) in this study presented evidence of congestive failure at the time of examination at the Mayo Clinic. Auricular fibrillation was present in sixty cases (38 per cent), occur-

TABLE VIII

RELATION OF RECURRENT RHEUMATIC FEVER TO AGE AT DEATH AND TO PERIOD FROM FIRST ATTACK TO DEATH

ATTACKS OF RHEUMATIC FEVER	AVERAGE AGE AT DEATH, YEARS	YEARS FROM FIRST ATTACK OF RHEUMATIC FEVER TO DEATH, (AVERAGE)
1	40	19
2	35	22
3	44	31
4	39	26
5	30	23
6	48	33
8	27	22

TABLE IX

RELATION OF RECURRENT RHEUMATIC FEVER TO SEX

ATTACKS OF RHEUMATIC FEVER	SEX	
	MALES	FEMALES
1	58	56
2	14	10
3	3	8
4	2	2
5	2	1
6	1	2
8		1

ring most commonly in Group I in which there were fifty-three cases; it was present at the time of examination in four cases in Group II and in three cases in Group III.

Fairly reliable data were obtained regarding the mode of death. One hundred forty-seven patients died a "gradual death," the majority presumably of congestive failure. Eight patients died suddenly, five of them from mitral stenosis, two from aortic stenosis, and one from aortic insufficiency. In four of the cases of mitral involvement there was clinical evidence of cerebral embolism. The patient with aortic insufficiency who died suddenly was thirty-six years of age. The left coronary artery was occluded by a thrombus arising from mural thrombosis of the left ventricle. Five patients died from subacute bacterial endocarditis.

SUMMARY

In this study of the course of 160 cases of rheumatic heart disease, it was disclosed that at the time of examination at the Mayo Clinic 81 per cent of the patients were less than fifty years of age. The disease occurred most commonly in the fifth decade, forty-seven cases (29 per cent). Only seventeen patients (19 per cent) were more than fifty. The sex incidence was equal, and no striking differences were found in a comparison of the data divided on the basis of sex. The first attack occurred before the age of thirty in 136 cases (85 per cent) and before the age of twenty in 103 cases (64 per cent). The primary infection occurred in only five cases (3 per cent) after the fortieth year. The average age at the time of death was thirty-two years.

The cases were divided into three groups for comparative study according to the clinical diagnosis of valvular involvement. In Group I with mitral involvement there were 124 cases, in Group II with aor-

tic involvement twenty-one cases, and in Group III with both mitral and aortic involvement, fifteen cases. In Group I, fifty-one patients were males and seventy-three females; the first rheumatic infection occurred before the thirtieth year in 106 cases (85 per cent), and in only three cases (3 per cent) was the first attack after the fortieth year. The average age at death was thirty years. In Group II there were nineteen males and two females; rheumatic infection occurred before the thirtieth year in seventeen cases (81 per cent); the average age at death was forty-three years. In Group III there were ten males and five females; in thirteen (86 per cent) the initial rheumatic infection occurred before the thirtieth year; the average age at death was thirty-two years.

Recurrent rheumatic infections were most prevalent in the first decade of life in which they occurred in sixteen cases (55 per cent). The greatest number of attacks in any one case was eight. There was no instance of recurrent infection after the thirtieth year. There was only one instance of recurrent infection in Group II. No constant relationship is revealed in this study between the number of attacks of rheumatic fever and the age at which death occurred. There is little difference between the incidence of recurrent infection in the two sexes. In sixty-two cases (39 per cent) there was congestive failure at the time of examination. Auricular fibrillation occurred in sixty cases (38 per cent). Death from gradual heart failure occurred in 147 cases, while sudden death occurred in eight cases. Five patients died from subacute bacterial endocarditis.

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VARYING VENTRICULAR COMPLEXES IN COMPLETE HEART-BLOCK*

An Account of a Postmortem Examination in One Case

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VARIATIONS in the form of the initial ventricular deflections (the QRS group) in the electrocardiogram are known to be produced by several factors of which perhaps the more important are the rate of the excitation wave and the course it pursues. The gradual development of defective intraventricular conduction leading to complete or partial bundle-branch block has frequently been recorded experimentally[1] and clinical curves of a similar nature are not lacking.[2, 3] The two cases here recorded are of interest in that the complete auriculoventricular dissociation was accompanied by the occasional spontaneous appearance of a succession of complexes each being intermediate in form as compared with its neighbors and varying in type between levo- and dextrocardiogram.

CLINICAL CASES

Case 1.—J. L. (Record No. 4432), male, aged seventy-seven years, a piano-maker, was admitted to the hospital of the Rockefeller Institute on December 10, and died on December 12, 1921. His complaint was shortness of breath, weakness, and cough. The family history was unimportant and the patient's wife did not know whether he had suffered from any serious infectious diseases except influenza in 1918. There is no reason to suppose that he had had syphilis though this fact could not be known. His habits were satisfactory.

In September, 1921, the patient had an attack of "grippe" and bronchitis which kept him indoors for two weeks. At that time he had fever and cough, expectorating moderate amounts. He returned to work before he had become completely restored to good health. Until November 15, he continued with his employment when he was forced to stop on account of dyspnea, and of feeling restless and weak. He had been unable to return to his work since that date. On walking about dizziness bothered him, and a little more than a week previous to his admission to the hospital his feet began to swell. His nights had been disturbed by restlessness and insomnia, and two days before admission he developed periods, especially on first waking, during which he was irrational. His pulse was known to have been slow for about five weeks, being about 35 per minute. He was given digitalis in the form of the infusion and then of tincture, but he refused to take it after a while; at all events what he took was said to do him no good. Headache had troubled him and for this phenacetin gave him relief. There was no history of convulsions, no syncopal attacks, no pain in the chest and no unusual degree of breathlessness.

*From the Hospital of the Rockefeller Institute for Medical Research, New York.

No period was noted in which it could be said that the pulse became unusually slow.

Physical examination revealed an old man lying in bed on about two pillows. He looked ill but not especially uncomfortable. The breathing was of outspoken Cheyne-Stokes character, but apparently caused him no distress. In the apneic intervals there was momentary loss of consciousness and the eyes closed. Breathing was then gradually resumed. There was marked cyanosis of the lips, hands, and feet. *The heart:* The apical impulse was situated in the fourth space, 12 cm. from the midsternal line. There was no thrill felt, and no diastolic shock. The heart rate was unusually slow (36) and the rhythm regular. The transverse diameter of the heart in the fourth space, was 15.8 cm. On auscultation slight accentuation of the pulmonary second sound was detected and also the presence of a systolic

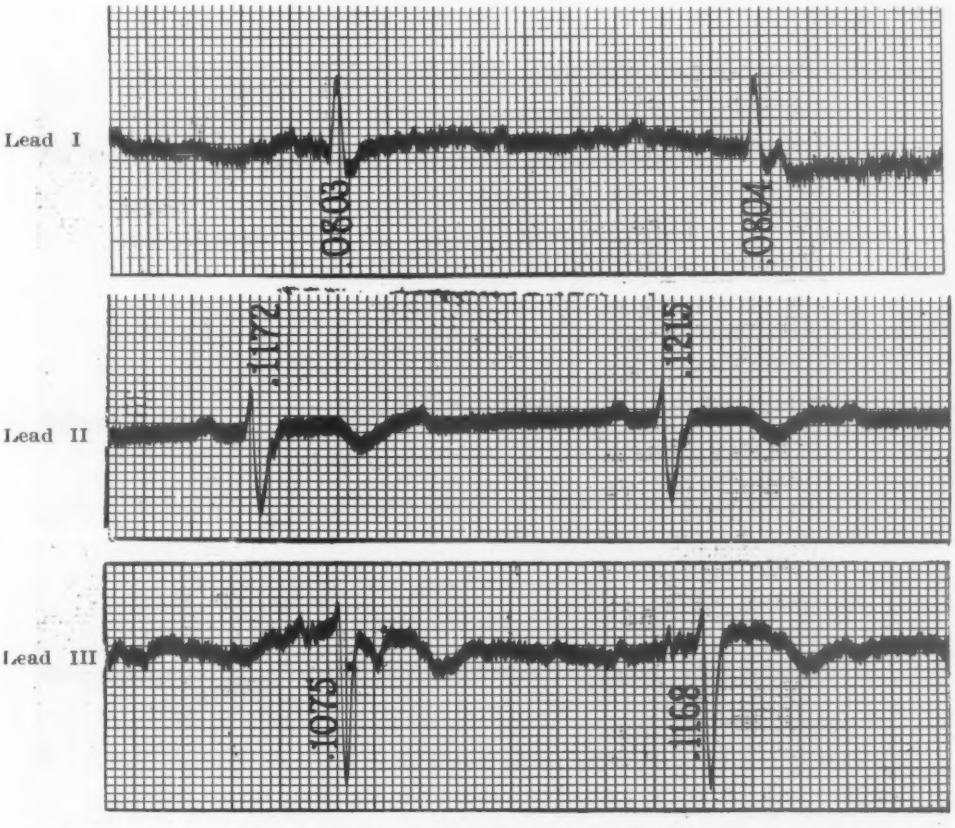

Fig. 1.—(Leads I, II, and III.) Shows an electrocardiogram made on Dec. 10, 1921. Complete heart-block is present. There is a preponderance of left-sided effects. The QRS time is prolonged above normal in Leads II and III. In Lead I, it appears to be within the normal limits, but accurate measurement is hampered by the presence of a tremor. The ventricular rate is 37.5 and the auricular rate is 62.5 per minute. These electrocardiograms were all taken so that divisions both of the ordinates and of the abscissae equalled 1 mm.

murmur at the apex. This was conducted for a distance of about 4 cm. into the axilla. *The pulses:* These were equal, slow, regular, of good force and volume. The arteries were thickened and there was a capillary pulse present. The blood pressure was 240 mm. systolic, 65 diastolic. Inspection of the neck vessels was unsatisfactory in that motions representative of auricular activity were not seen. The *lungs* were resonant throughout but showed the presence of a few coarse râles and sibilant and sonorous rhonchi. The *abdomen* showed no abnormality. The flanks were tympanitic but liver dullness extended to 3 cm. below the free border of

the ribs. There was no tenderness detected. The legs showed edema of the dependent portions and over the lower three-quarters of the pretibial region.

On the night of December 10 he became irrational and was restrained with difficulty. He had had veronal. Until his death on December 12, he was practically unconscious. After being given morphine the Cheyne-Stokes breathing disappeared being replaced by stertorous more or less regular breathing. A curious phenomenon noted during the Cheyne-Stokes breathing was the rigidity of the muscles of the trunk and especially of the arms, during the apneic periods, and the holding of the extremities in fixed positions extended at right angles to the trunk or at positions approximated to this. His general condition gradually became worse, the pulse sometimes not being felt at the wrist for prolonged periods, and this was accompanied by the development of apnea and great cyanosis. In one of these spells the patient died.

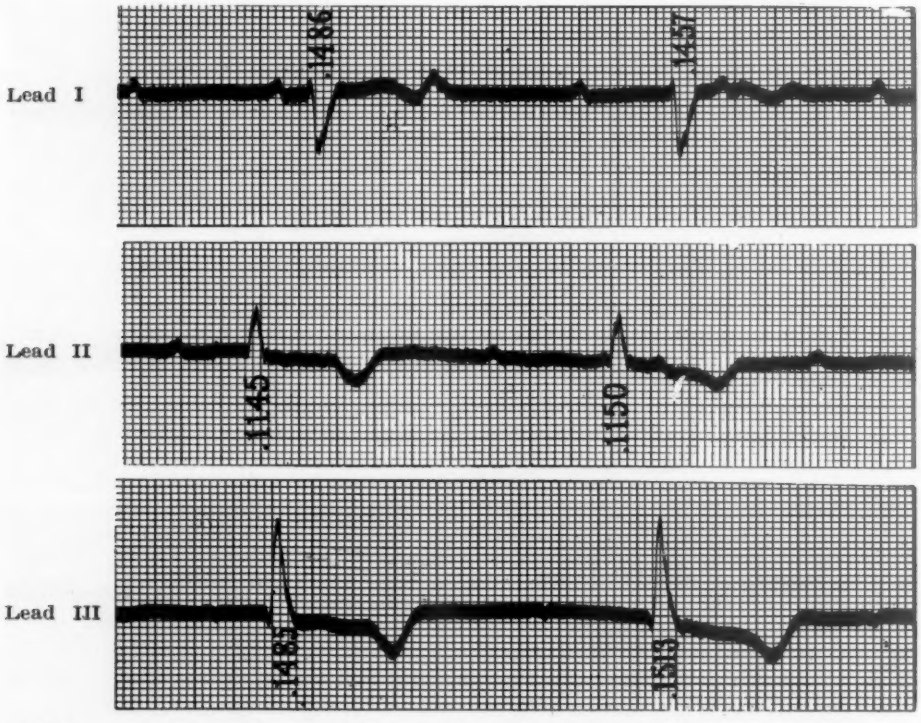

Fig. 2.—(Leads I, II, and III.) Shows an electrocardiogram made on Dec. 11, 1921. The complete heart-block persists, but right-sided effects now preponderate. The QRS time is prolonged in all leads, and the complexes indicate defective conduction by the left bundle-branch. The ventricular rate is 32.4 and the auricular is 77.4 per minute.

Electrocardiograms were made on nine occasions on the three days during which the patient was under observation. The first electrocardiogram was made at 12:15 P.M. on December 10 (Fig. 1), and demonstrates the presence of complete heart-block, the ventricular rate being 37.5 and the auricular 62.5 per minute. There is marked *left ventricular preponderance.* The next electrocardiogram (Fig. 2) taken at 11:45 A.M. on the following day (December 11) is noteworthy in that there is a complete change in the form of the ventricular complexes. Complete heart-block persists, but now the *dextrocardiogram*

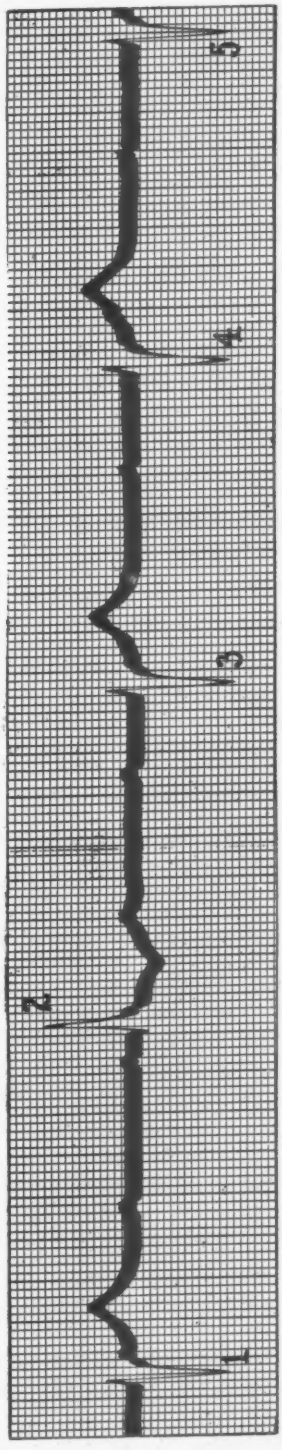

Fig. 3.—(Lead II.) Shows one sudden transition in the form of the ventricular complex. The second in the figure is the result of a preponderance of right-sided effects; the remainder show predominant left-sided effects. This single systole is not a premature contraction. The change in the form of the complex is remarkable in that one in virtually the mirror image of the other.

predominates and the complexes assume the form associated with a lesion of the left bundle-branch. One gram of digitan was administered orally to the patient this day, but this record was made before any of the drug had been given. On December 12, a further series of records was made and these showed that the ventricular complexes had returned to their original form, that is to say, left-sided effects preponderating. There were, however, exceptions to this, and Fig. 3 shows an abrupt alteration in the form of the electrical response, the second complex in the figure being diametrically opposite to those preceding and following it. This complex is of the type associated with a right preponderance. The others in the figure suggest a left preponderance. In Fig. 4 is reproduced another record taken on the same day (Dec. 12). This electrocardiogram is remarkable in that it shows the *gradual* transition from one preponderance to the other. The record commences with two successive complexes illustrating the predominance of the dextrocardiogram. These are of constant form. The fifth, sixth, and seventh complexes also appear uniform in type, but the main deflection is now directed downwards. For these three cycles the levocardiogram dominates. The third and eighth complexes are intermediate in form between the fully developed right and left effects. After three heart beats the mechanism returns to the original right-sided preponderance, one complex, intermediate in type, again intervening. This gradual transition in the form of the complexes was observed on the day following the administration of the digitan.

Abrupt transitions in the form of the ventricular response, as described above and shown in Fig. 3, were known to be occurring frequently on the morning of December 12, before the atropine test was performed. They persisted after grain $\frac{1}{50}$ had been given intravenously. The injection of atropine was followed by auricular acceleration but failed to release the block.

A postmortem examination was performed December 13, eighteen hours after death. Only the essential findings will be described. The peritoneal cavity was found to be normal. There was no fluid present. On opening the thorax a large precordial surface was exposed. In the right pleural cavity there was about 1,000 c.c. of straw-colored fluid in which were many flakes of fibrin. The left lung was firmly bound down at the apex by two bridges of fibrous tissue. *Lungs:* The right was somewhat congested but was otherwise normal. The left was firmly bound down by adhesions, and about the junction of the lower and upper lobes on the anterior aspect of the lung there was a hard calcified plaque from which fibrous tissue extended into and over the lung in a stellate form. On section the lung appeared dark in color and quite fibrous throughout. The pleura was distinctly thickened.

The *liver* weighed 1750 grams. The surface was roughened and presented the characteristic appearance of sclerosis. Cut section presented the typical appearance of chronic venous congestion.

The *kidneys* were alike. On stripping the capsule a finely granular surface was exposed, and a few retention cysts were present. The cortex was seen to be slightly diminished in thickness. The pyramids appeared normal.

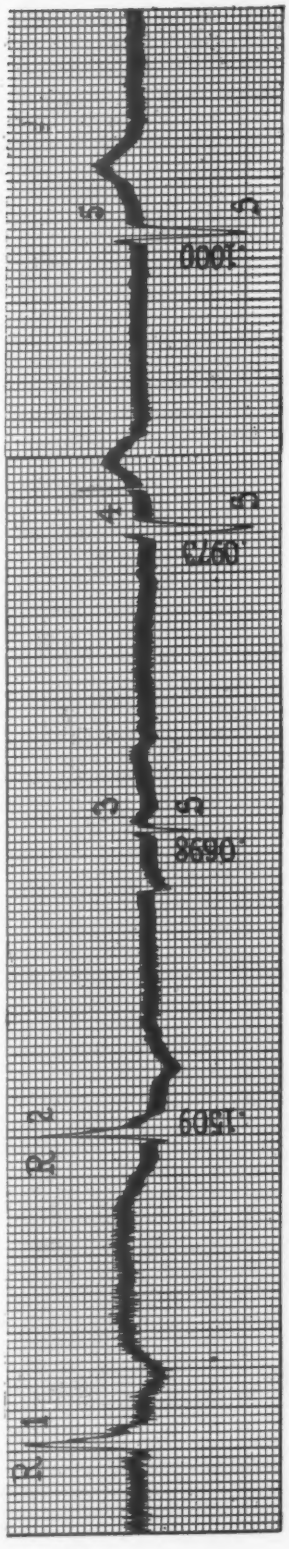

Fig. 4.

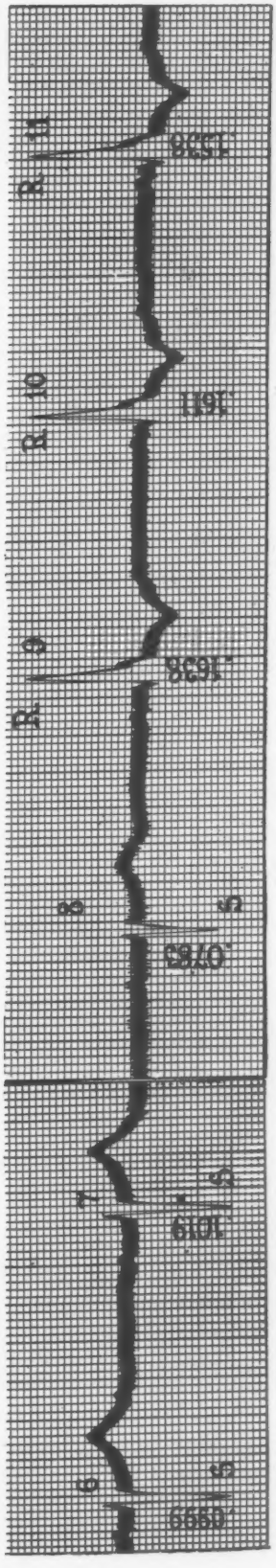

Fig. 4 (continued).

Fig. 4.—(Lead III.) This curve illustrates a gradual change in the form of the ventricular complex. A definite preponderance of left-sided effects is shown by the form of the complex in the fourth to the seventh systoles. This rhythm is preceded and succeeded by single complexes (the third and the eighth) intermediate in type between fully developed right and left effects. The ventricular rate is 40 per minute.

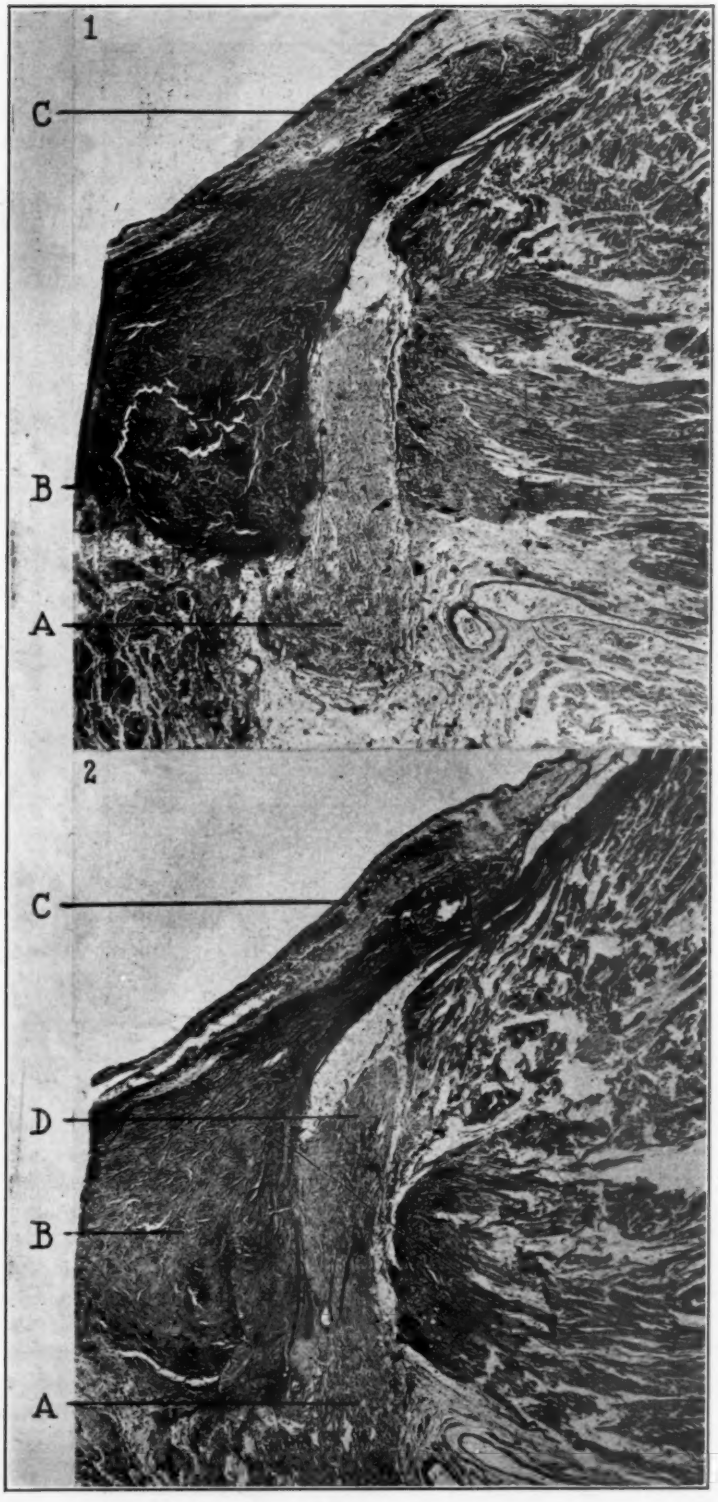

PLATE I

Fig. 1 (Slide 105).—Shows the auriculoventricular node in its passage through what seems to be a cleft in the central fibrous body. (X15.)

Fig. 2 (Slide 116).—Shows the node together with the beginning of the main stem of the bundle on its passage forward close to the endocardium of the left ventricle. (X15.)

The stomach, intestines, and bladder were not examined. The suprarenal capsules presented no abnormality.

The *aorta* showed a marked degree of general arteriosclerosis. There was no lesion seen in the *heart** to which could be attributed the presence of heart-block. There was no tumor or calcareous nodule in the region of the upper portion of the interventricular septum. The heart muscle was friable and on cut section showed little more than the expected amount of connective tissue about the blood vessels.

Measurements:	Transverse diameter just below A-V groove	13.5 cm.
	Long diameter from A-V groove to apex, anteriorly	10.0 cm.
	Long diameter from A-V groove to apex, posteriorly	10.5 cm.
	From base of auricles to apex, posteriorly	16.5 cm.
	From A-V groove to auricles	7.0 cm.

There was a great deal of fat over the right auricle and conus. No obvious lesion of the outer surface of the heart was seen and there was no evidence of thrombosis or embolism of the coronary arteries from the outside. No infarct or aneurysm of the heart was detected.

The thickness of the wall of the left ventricle at the level of the papillary muscles, exclusive of fat, measured 18 mm., apex 6 mm., base (1 cm. below the A-V groove) 14 mm.

The mitral valve admitted the tips of three fingers comfortably; it showed distinct atherosclerotic thickening at its base.

The corpora arantii of the pulmonary artery were slightly thickened and showed a few fenestrations. There was slight sclerosis just below the valve attachments. The tricuspid valve admitted four fingers comfortably. The aortic valve showed no real deformity, but there was atherosclerosis, especially of the corpora arantii. The undefended space was translucent. The coronary vessels showed in their course, patches of atherosclerosis, which became less numerous as the vessels were followed towards their terminations.

Microscopical: A block of tissue was cut from the septum of the heart in the neighborhood of the undefended space so as to include the anterior lip of the coronary sinus. It extended forward far enough so that a portion of the septum in front of the undefended space was also included. This block was cut in serial sections 10 micra thick, the section running at right angles to the long axis of the heart. Every fifth section was mounted for staining. The auriculoventricular node, as well as its auricular connections, was easily identified lying, when it first came into view (the sections having been cut from above downwards), above and to the right and behind the central fibrous body. It passed in the usual way forward and towards the left side so as to come to lie under the endocardium of the left ventricle. Its point of division was also identified. The bundle cannot be said to have been interrupted at any point in its course. The main stem was, however, in comparison with the node and in comparison with the left division, much attenuated. In the main stem although muscle fibers could be seen they were exceedingly few in number. The rest of the tissue of which it was composed consisted, for the most part, of dense fibrous tissue. At the point where the right branch passed off from the main stem there were a number of large thin-walled veins. As far as the right branch was traced it was, like the main stem, composed almost entirely of connective tissue dense in appearance, in the meshes of which a few muscle fibers could be traced. The appearances are illustrated in the accompanying series of microphotographs (Plates I and II).

Although it cannot be said that interruption of the continuity of the bundle had taken place there can be little doubt that in its

*The pathological examination of the heart was made by Dr. Cohn.

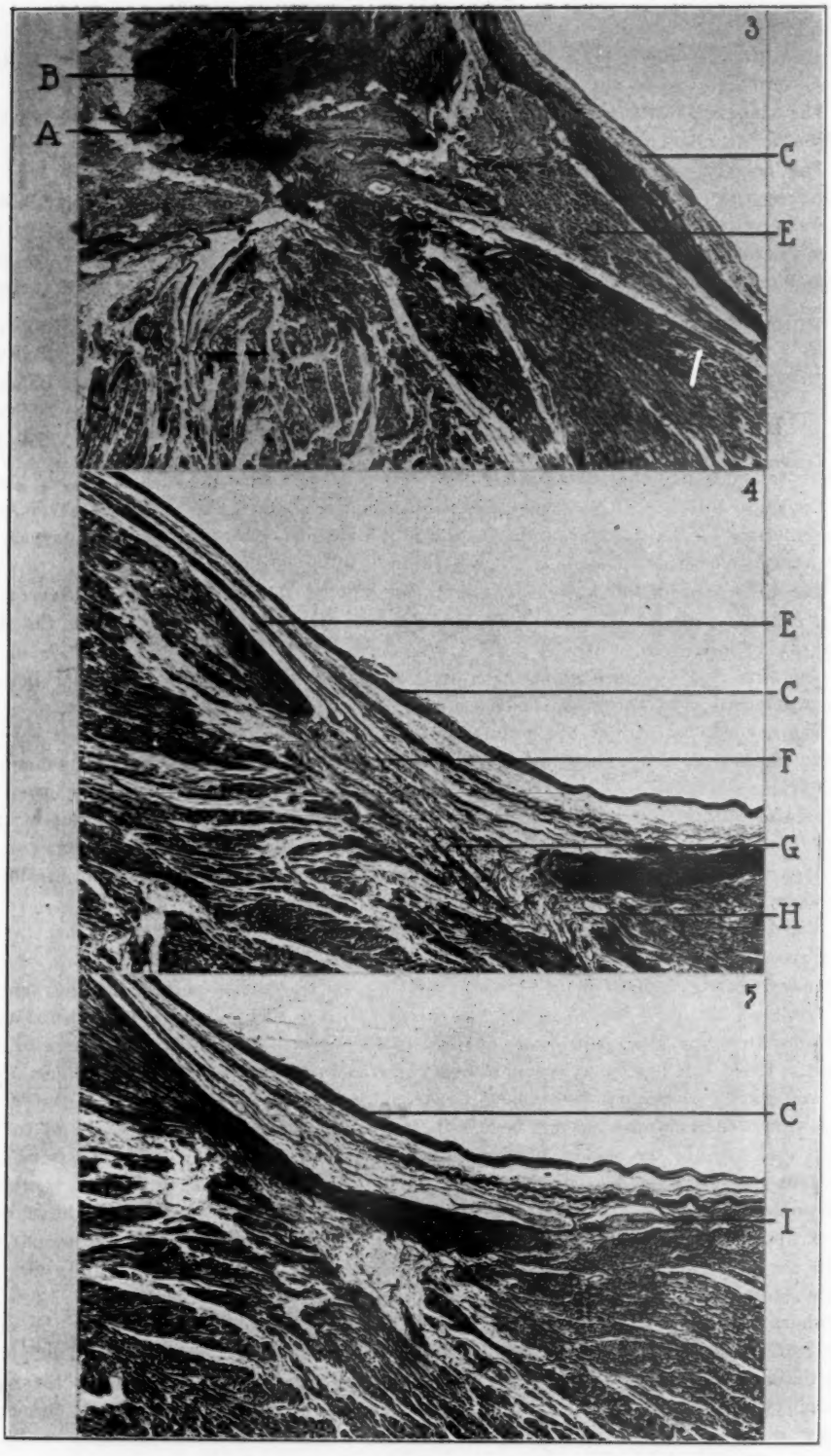

PLATE II

Fig. 3 (Slide 127).—Shows the main stem of the bundle to about half of its length under the lining of the left ventricle. The node can still be seen posterior to the central fibrous body. (X15.)

A is the auriculoventricular node; *B* is the central fibrous body; *C* is the endocardium of the left ventricle; *D* is the beginning of the main stem of the bundle of His; *E* is the main stem of the bundle; *F* is the bundle at the point of division; *G* is a vein cut longitudinally; *H* is the right division of the bundle; *I* is the left division of the bundle.

sclerosed state the ability of the few muscle fibers that were left to conduct impulses must have been reduced.

CASE 2.—P. O. (Record No. 5871), male, aged fifty-three years, an engineer, complained of attacks of dizziness and swelling of the feet. The family history was of no importance and he gave no history of any rheumatic or other infection except the common disorders of early childhood. He had a mild attack of dry pleurisy some years ago. His present illness commenced suddenly on July 30, 1926, when on walking a short distance he experienced a dizzy sensation, everything went black before his eyes, and he fell and lost consciousness. Up to that time he had felt perfectly well and able for his work. After a few minutes consciousness was regained. Following this experience he was kept confined to bed for a month. During the first week that he was in bed he had repeated attacks similar to the first one, as a rule two or three a day, some lasting only a few seconds, others for a minute or two. He described the seizures as starting with a buzzing noise in the head located particularly in both temporal regions. The temporal muscles seemed to vibrate and following this, blackness appeared before his eyes and he could feel his head roll over to one side and consciousness was lost. He was not aware of any twitching in the muscles of the arms or legs. By the end of the month's rest in bed he was feeling distinctly stronger and seizures only occurred about once in two weeks.

He was examined at the hospital of the Rockefeller Institute on September 15, 1926. The presence of complete heart-block was discovered and the Wassermann reaction of the blood was strongly positive. Active antisyphilitic treatment* was commenced in October. This consisted of eight injections of 0.2 gram bismuth intramuscularly at weekly intervals, accompanied by daily doses of potassium iodide.

His last attack occurred on November 2, and his progress was uneventful until about January 5, 1927. Edema of the ankles was then noticed.

On January 13, he was admitted to the hospital. His only complaint then was that he was more readily fatigued than formerly. The swelling of the feet had persisted since it was first noticed.

Physical Examination: The patient was a thin spare subject, poorly nourished and underweight for his height. Breathing was not embarrassed. There was no cyanosis and no distress. The eyes, ears, nose, and throat appeared healthy. There was some slight infection of the teeth with pyorrhea alveolaris. The tonsils were small. The thyroid gland was not enlarged. *Chest:* The thorax was poorly covered. The ribs were prominent in the upper part of the chest and were indrawn in the lower axillary regions. *Heart:* The apex beat was seen to be 8.3 cm. from the median line in the fifth space. The heart rate was slow (28 per minute), and there was a prolonged localized apical thrust. No thrill or shock was felt. The area of cardiac dullness was 6 cm. to the right and 11 cm. to the left from the mid-sternal line in the fourth space. The outer border of cardiac dullness was 11.5 cm. to the left in the fifth intercostal space. A soft blowing systolic murmur completely replaced the first sound at the apex. This was heard a short way into the axilla but not elsewhere. The murmur was occasionally absent for a single cardiac cycle, being replaced by a thudding first sound. This was attributed to

*We are indebted to Dr. Edgar Stillman for his cooperation in carrying out antisyphilitic treatment.

Fig. 4 (Slide 133).—Shows a fairy long stretch of the main stem of the bundle lying under the endocardium. It presents the appearance of a thin fibrous cord. It also shows the bundle at the point of division. A vein cut longitudinally is here to be seen. Farther forward and to the right is the dense fibrous cord of the right division in which a few muscle fibers can be identified. (X15.)

Fig. 5 (Slide 136).—Shows the left division of the bundle under the endocardium of the left ventricle. Here the dimensions of the bundle are greater than at any other point between here and the node. (X15.)

the coincident contraction of both auricle and ventricle. The second sound was pure. There was no diastolic murmur heard. The second pulmonary sound was not accentuated. No evidence of auricular contractions was heard over the precordium, but small frequent regular waves could be seen in the jugular vessels in the neck and this in the absence of a corresponding apical thrust. *Pulses:* The pulses were equal in force and time. The radial beat was large, full, and well sustained. The arteries were palpable, thickened, and had some slight tortuosity. The blood pressure was 140 mm. systolic and 80 diastolic. *Lungs:* Expansion was good and the patient had no difficulty in taking a full deep breath. There was a markedly hyperresonant note over both lungs. The breath sounds were vesicular, with some prolongation of expiration. No moist accompaniments were heard. *Abdomen:* Examination revealed nothing abnormal. There was no tenderness detected on palpation. The liver was of normal size; the lower pole of the spleen was not felt and there was no ascites. *Extremities:* At the time of his admission there was a trace of edema around both ankles. This soon disappeared with rest in bed. There was no clubbing of the fingers or toes. The superficial veins were not unduly distended. *Nervous system:* No abnormality in the superficial or deep reflexes was detected. The Argyll Robertson pupil reaction was absent. Romberg's sign gave a negative response. There was no ataxia, and no sensory disturbance.

On January 14, renal function tests were performed. The plasma nonprotein nitrogen was 29 mg. per cent. The phthalein output was 65.1 per cent in two hours. The Van Slyke urea index was 38.3. The blood creatinine was 1.76 mg. per cent. These results are all within normal limits. There was a trace of albumen in the urine but no casts or other abnormality were detected.

His response to 1.7 mg. of atropine sulphate injected intravenously was tested on January 18, and again on March 14, 1927. The drug caused definite acceleration of the auricular rate, but had no effect on that of the ventricles, complete heart-block persisting. The injection of adrenalin (0.3 c.c. subcutaneously—1/1000 solution) induced slight ventricular acceleration, the rate rising from 38 to 43 per minute, and a coincident but transient rise in systolic blood pressure from 138 to 162 mm. Barium chloride, 30 mg. given by mouth at four hour intervals during the day for eight doses, appeared to raise the inherent ventricular rate from 36 to 42 per minute.

The patient was discharged on January 31, 1927, and allowed to resume his employment. He had no Adams-Stokes attacks while under observation and the slight cardiac decompensation present when he was first a patient had rapidly subsided. Since then he has reported for examination frequently and has remained in good health. Antisyphilitic treatment of the type described above has been continued with no ill effects, and the patient has remained able for his work. On June 5, he had a transient attack of loss of consciousness. This only lasted for a second or two and he was able to go on with his work. Two similar attacks occurred the following day. There has been no change in the physical signs and the electrocardiograms show that the complete dissociation of auricles and ventricles continues as before. The patient was readmitted to the hospital on June 21, for further observation. Exercise sufficient to produce slight dyspnea and general discomfort was without effect on the ventricular rate. No change was observed in the form of the complex. The administration of digitan (1.10 gm. in 12 hours) though sufficient to induce slight headache and anorexia, had no definite influence on the idioventricular rate. The form of the complexes remained unchanged. When last seen on June 23, the patient was in good health and able to be engaged in his usual employment.

The electrocardiograms of this case are shown in Figs. 5, 6, 7, 8 and 9. They are similar in type to those described in connection with

the previous case. Fig. 5 demonstrates the findings when he was first seen on September 15, 1926. Complete heart-block is present, the ventricular rate being 35 and the auricular 77. The dextrocardiogram predominates. After his admission to the hospital many records showed a similar state of affairs to be present and it was not until January 21 (after he had been under observation in the ward for a week and his general condition much improved) that a complete change was detected in the character of the electrocardiogram. This

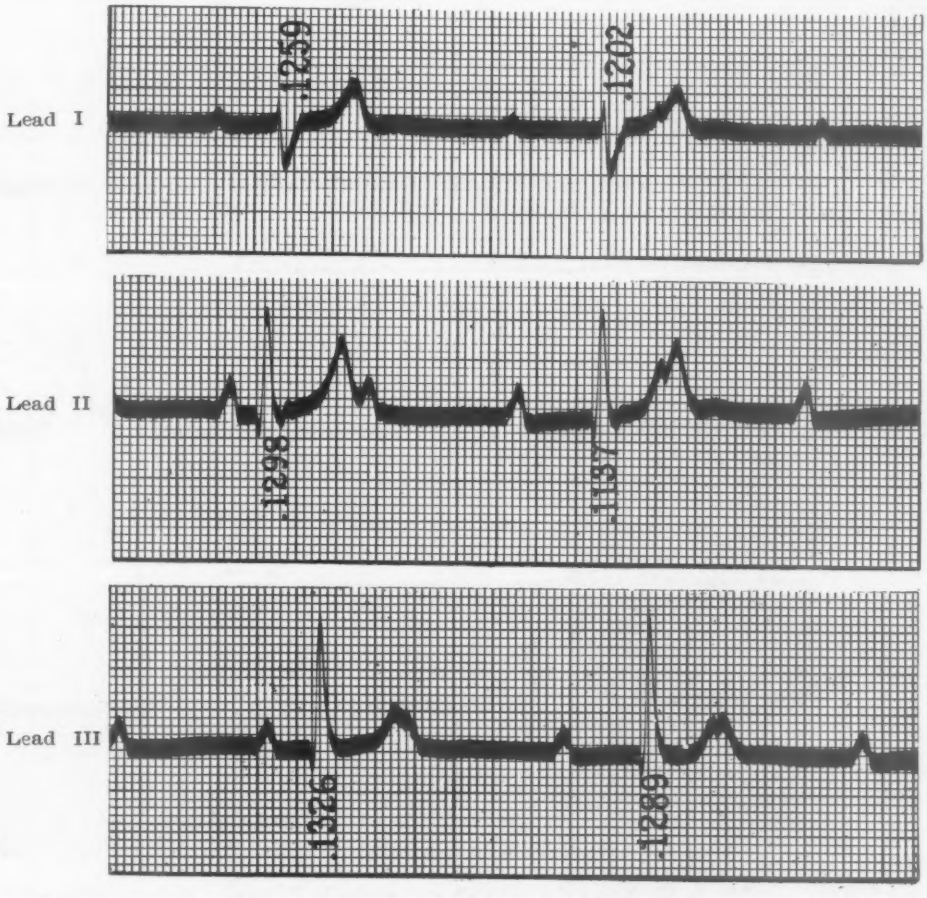

Fig. 5.—(Leads I, II, and III.) Complete heart-block with a preponderance of right-sided effects. The QRS time interval is prolonged above normal in all leads. The ventricular rate is 35; the auricular, 77.

is shown in Fig. 6, in which, in contrast to Fig. 5, the levocardiogram predominates. The auriculoventricular dissociation persists. The main deflections are reversed, but the T-waves remain positive as they were on previous occasions. Their amplitude however is altered, being less in Lead I and greater in Leads II and III. The ventricular rate is 28, the auricular, 63. That this abrupt alteration in the form of the electrocardiogram was not due to any technical error, that is to say in the misapplication of the electrodes, is proved beyond doubt by the

electrocardiogram recorded the following day, January 22, in which is depicted a period of transition from one preponderance to the other (Fig. 7). The first two complexes with which the record commences exemplify the usual type found in this patient in Lead III. The main deflection is positive. The last complex (No. 6) at the extreme end of the record is reversed in direction, the main deflection being negative. The intervening cycles (Nos. 3, 4, and 5) are of considerable interest, adjacent complexes being intermediate in character between the fully developed dextrocardiogram and levocardiogram of this subject. Com-

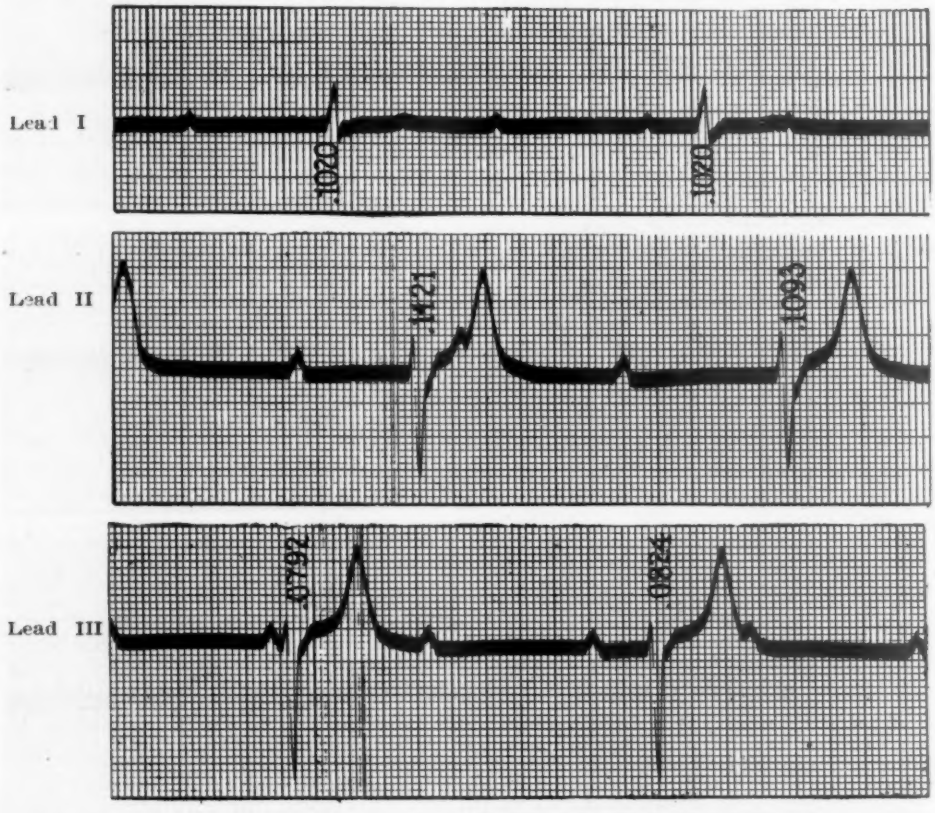

Fig. 6.—(Leads I, II, and III.) Shows predominant left-sided effects. The QRS time is slightly prolonged except in Lead III. This may be only apparent on account of the selection in making the measurement of a point on the upstroke of *S*, before the string had returned to the base line. The ventricular rate is 28; the auricular, 63.

paring the complexes marked 2 to 6 it is seen that with succeeding systoles the R-wave becomes progressively smaller in amplitude and with this change the S-wave becomes sharper and gradually steeper until the complex No. 6 is reached. With the decreased preponderance of the dextrocardiogram the QRS time diminishes from 0.1621 second in complex No. 1 to 0.0660 second in complex No. 4. As the levocardiogram develops the intraventricular conduction time increases again until in the last complex of the record it has reached a period

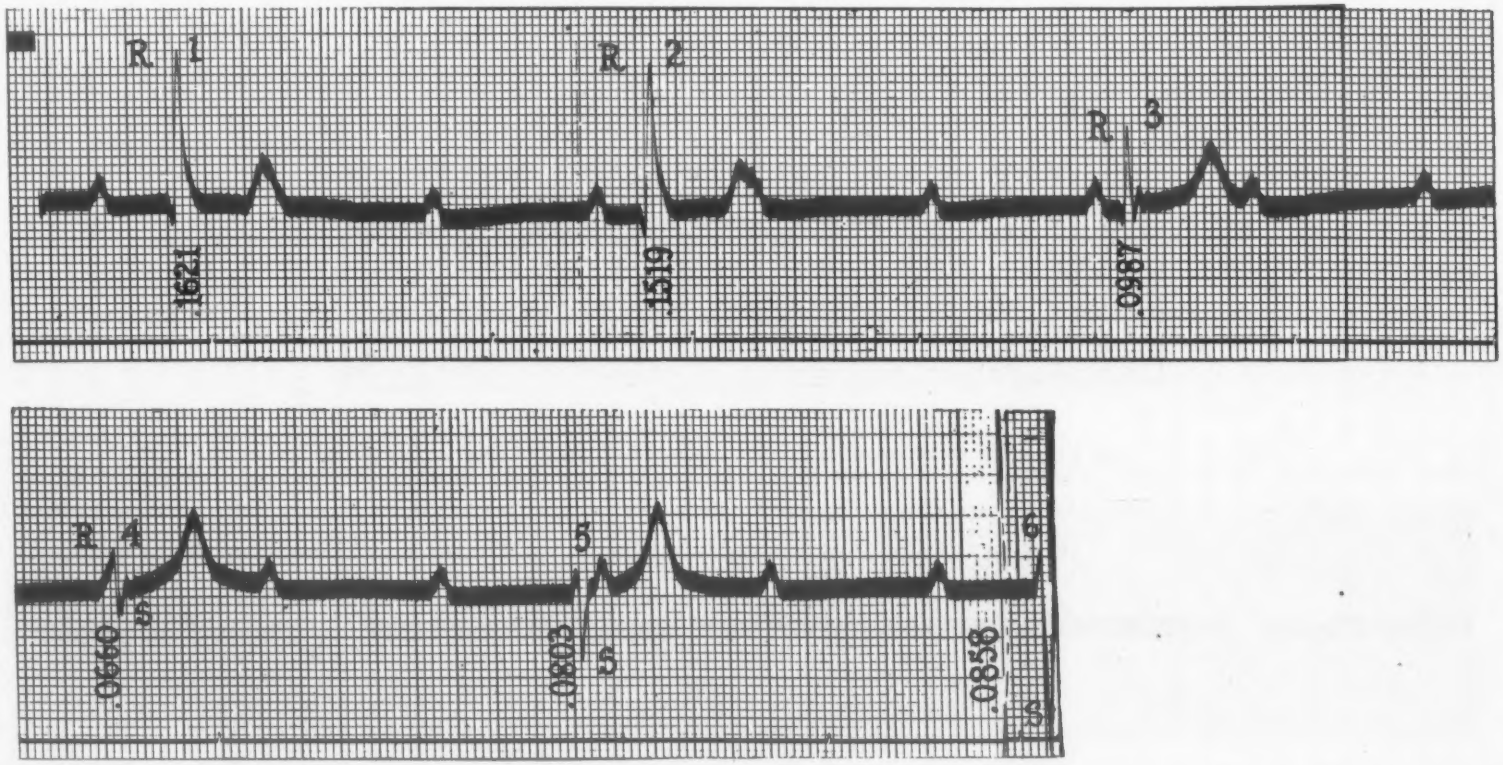

Fig. 7*.—(Lead III.) This record shows a gradual transition in the form of the ventricular complexes from dextrocardiogram by stages to levocardiogram. The QRS intervals are: Complex 1=0.1621; 2=0.1519; 3=0.0987; 4=0.0660; 5=0.0803; 6=0.0858. The ventricular rate is 25 per minute.

*In preparing this record for publication, the portion of film bearing the final complex (No. 6) was inadvertently cut and detached from the rest of the record. It has been printed and replaced as nearly as possible in its correct time relationship.

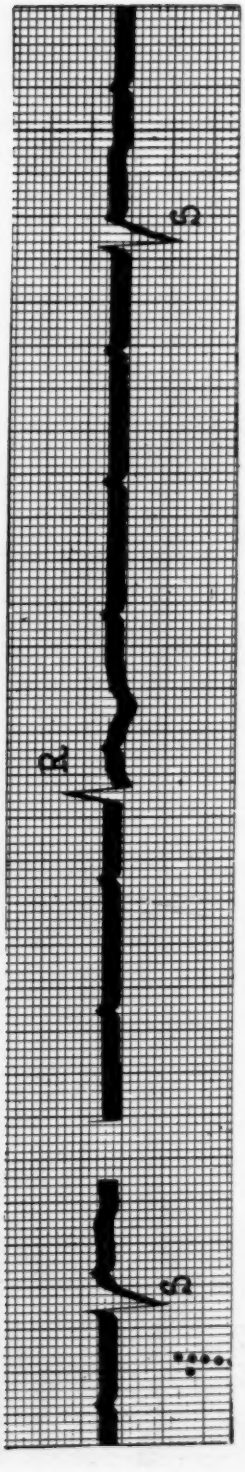

Fig. 8.—(Lead I.) A regular succession of complexes with right-sided effects predominating is shown to be momentarily interrupted in this record by a single beat with predominant left-sided effects.

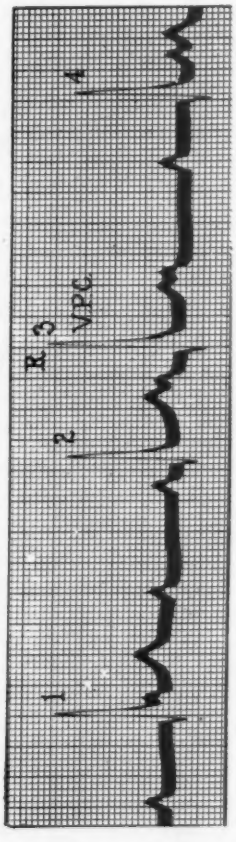

Fig. 9.—(Lead III.) Shows the presence of right-sided premature contraction.

of 0.0858 second. The ventricular rate over the whole period of the record is 25 per minute; the auricular is 76. In another record which showed a similar gradual transition in the form of the complexes over a short period of time the ventricular rate was 24.5. He had received none of the digitalis preparations before these electrocardiograms were made. Abrupt transitions were also noted in this case both before and after the administration of atropine. An example of this occurring in Lead I is seen in Fig. 8. The second complex in the record differs from the others in that the main deflection is directed upwards. Superficially this beat resembles an extrasystole in that it occurs prematurely, but only by 0.10 second. It resembles very closely the type of complex present in this subject when the levocardiogram predominated (compare Fig. 6), save for the fact that it is more definitely diphasic in type. The T-wave is negative; whereas in Fig. 6, the T-waves are faintly positive. This may possibly be an unjustifiable comparison because the T-waves accompanying the remaining complexes in Fig. 8 are not so prominent as those in Fig. 5, and yet the direction of the main deflection is the same. Premature beats of right-sided origin were, however, very occasionally observed in this patient and in form they differed only slightly from the complexes typical of right-sided preponderance. An example is shown in Fig. 9. The third ventricular complex in this record is of premature origin and conforms to the general rule for extrasystoles in complete heart-block in that the returning cycle after the premature beat is equal in time to the cycles of the idioventricular rhythm immediately preceding it. Comparing it with the other complexes in the record, the main distinction is that the R-wave of the premature contraction is of greater amplitude. In its general form and time relations it is very similar to the dextrocardiogram as it occurs in this subject. This record was secured during an atropine test and the auricular acceleration can be detected in the figure.

LITERATURE

There are few published observations on similar cases to be found in the literature though the result of a lesion of the main conducting tract and the syndrome associated with it is of common occurrence and well recognized.

The first example was reported by Cohn[4, 5] in 1911 and described more fully in 1913. In this case (occurring in a patient seventy years of age) complete heart-block was only transient and was probably due to the administration of digitalis. Electrocardiograms revealed the presence of gradual changes in the form of successive ventricular complexes varying through many stages from dextrocardiogram to levocardiogram. This phenomenon lasted for a few days. Shortly afterwards the cardiac rhythm returned to normal and persisted so

for two years. Cohn suggests that the variation in the complexes may be due either to functional depression of the bundle-branches or to dislocation of the center of impulse production now to one side of the heart, now to the other. These suggestions seem adequate to explain the intermediate complexes if it be assumed that the degree of functional depression varied asynchronously in the two branches in the one case, or in the other that two centers of impulse production, one on either side of the heart, were simultaneously competing for control of the inherent rhythm. Oppenheimer and Williams[6] recorded a case in an old hemiplegic subject, who showed frequent changes in the ventricular complex from beat to beat. Complete heart-block was present, but serial sections of the conducting tract failed to reveal an organic lesion. As an explanation for the anomalous complexes they discuss the question of changes in the site of the pacemaker and also suggest that the mechanism might be accounted for by variations in the rate of conduction of the excitation wave to either ventricle. Mathewson,[7] in reporting four cases of defective bundle-branch conduction, describes one case in which the excitation wave was apparently conducted at times by the right branch, at times by the left branch and sometimes normally by both branches simultaneously. No complexes transitional in form between the levocardiogram and the dextrocardiogram are described and complete heart-block was not present. Christian[8] has reported four cases showing variations in the form of succeeding ventricular complexes which he attributed to digitalis intoxication. Necropsy was performed in one case. There was no evident lesion of the conduction system. Robinson,[9] in describing a series of cases showing aberration of the ventricular complex, reports upon one case of complete heart-block with a rhythmic variation in the form of the complexes. Alternate beats had the appearance of right bundle-branch block, the intervening ones being normal in form for this patient. There were also frequent transitions between these two main types. This phenomenon was noted to coincide with improvement in the patient's general state and by way of explanation it is suggested that the spread of the impulse was either not always complete or was not at the same rate through each ventricle. Wilson[10] has studied the influence of the vagus nerves on various forms of heart rhythm. In two subjects it was possible to produce right bundle-branch block by vagal stimulation. His Fig. 24 shows a gradual transition from right to left bundle-block. This was observed during the course of an atropine test. There was obviously no organic lesion of the conducting system in this patient though A-V rhythm with right bundle-branch block occasionally occurred spontaneously and could be produced by vagal stimulation. It was possible to bring about a reversal to normal rhythm and to restore conduction through the right branch by the use of atropine. Krumb-

haar[2] mentions one case of transient complete heart-block in which variation in the form of successive ventricular complexes was noted during the use of digitalis. This phenomenon disappeared with the restoration of conduction. Korns[11] has reported one case which, as regards the form of the ventricular complexes, is strikingly similar to the two cases described in this report. His patient suffered from rheumatic heart disease with arteriosclerosis, auricular fibrillation with a high degree of atrioventricular block, and congestive failure. When the many abrupt and gradual transitions from levocardiogram to dextrocardiogram were recorded the heart was deeply under the influence of digitalis, bigeminy being frequent. The patient recovered. To explain the curious forms of the ventricular complex, Korns advances the theory that the refractory periods of the branches are of unequal length, the relative degree of delay in the two branches varying constantly from cycle to cycle. He suggests that digitalis by prolonging the refractory period of the A-V node above that of the branches may permit their powers of conduction to recover, or on the other hand, it is equally possible, that in certain hearts, incapable of responding satisfactorily to the drug, digitalis may prolong intraventricular conduction time by lengthening the refractory period of the bundle divisions above that of the A-V node. Wilson and Robinson[12] have published a record showing a gradual change in the form of the ventricular complex occurring after the administration of a massive dose of digitalis in a patient with complete heart-block. Stenström[13] has described the findings in a man twenty-four years of age suffering from auricular fibrillation. Completely aberrant complexes varying in character between dextrocardiogram and levocardiogram were frequent. The peculiar form of the complexes is attributed to the activation of each ventricle by impulses which arise almost simultaneously one on each side of the heart. De Graff and Weiss,[14] in a study of eight cases of complete heart-block, noted in one a change in the form of the ventricular complexes on two occasions after the injection of epinephrin. Fifteen minutes after the drug had been given the direction of the main deflection became reversed and did not return to the original type for 165 minutes. Abrupt and gradual transition in the type of adjacent complexes are visible in their Fig. 2. White and Burwell[15] describe a case of auricular fibrillation in which there was marked variation in the shape of the initial ventricular complex from beat to beat. With the use of digitalis and the coincident improvement in the patient's health the complexes became more normal.

Cases strictly similar to the two forming the basis of the present study are those reported by Cohn, Oppenheimer and Williams, Christian, Krumbhaar, and Korns. This review of the literature, therefore, reveals the recording of eight cases in which there was a gradual

change in the form of successive complexes. It is significant that in all these there was auriculoventricular dissociation with a slow ventricular rate. It would seem probable that the phenomenon described might follow the administration of digitalis or occur as readily spontaneously. Variations in the configuration of the initial ventricular deflections of the electrocardiogram over long periods of time have frequently been noted. The gradual development of complete and partial bundle-branch block has been studied in several patients by various observers but a different mechanism must underlie the production of relatively sudden changes in the form of successive complexes as described in the instances mentioned above. It is not unnatural, therefore, to turn to experimental findings in order to seek an interpretation of the problem.

It was first shown by Eppinger and Rothberger[16] that section of both branches of the bundle of His does not produce standstill of the ventricles except for the space of a few moments. Soon after the lesions are made the ventricles recommence to beat in response to one of the lower centers which assumes the rôle of pacemaker. Wilson and Herrmann[1] found that after section of both divisions of the bundle, the returning ventricular contractions might have complexes with dominant right-sided effects, indicating a right-sided pacemaker or with dominant left-sided effects, indicating a left-sided pacemaker or finally the complexes might be of relatively normal outline indicating that the normal complex was the result of the simultaneous activity of two pacemakers, one in either bundle division below the point of destruction. In four out of five experiments these observers found occasional changes in the location of the pacemaker from one side of the heart to the other. These shifts were usually accompanied by complexes of transitional form (see their Fig. 20). Wilson and Herrmann conclude that complete heart-block associated with ventricular complexes of varying form is usually due to bilateral lesions of the bundle-branches and not to block of the main stem of the bundle of His. This theory obviously bears a close relationship to the clinical cases described above.

It is not, of course, justifiable to assume that clinical curves, displaying such peculiarities, indicate bilateral organic lesions of the bundle-branches for the same effects might as readily be produced by functional depression of conductivity and indeed in Cohn's original case complete heart-block was a temporary disturbance, normal conduction being regained. It is, therefore, necessary to consider the effect on the electrocardiogram of delayed conduction through one or the other of the bundle-branches.

It is due to the work of Lewis[17] that we have now an understanding of the formation of the QRS deflections of the electrocardiogram. He has found that the curve so described is really composite and is due

to the summated effects of the right and left ventricles. He has shown that in complete right bundle-branch block the resulting curve is written in its initial half by the left ventricle, and in the presence of a left-sided lesion by the right ventricle. If the resulting dextrocardiogram and levocardiogram be added together algebraically in their correct time relations, then a curve virtually identical in amplitude and time with the initial part of the normal ventricular deflections is formed. Wilson and Herrmann[1] point out that, as a result of this knowledge, it is clear that the effect of a lesion which delays without completely interrupting the passage of an impulse through one of the main divisions of the bundle will be an alteration in the ventricular deflection and that moreover this will consist in a shift in the time relations of right and left ventricular effects. They found that, by shifting the relative positions of dextrocardiogram and levocardiogram, it was possible to produce at will composite curves varying from the normal QRS complex to the complex of bundle-branch block curves. By an ingenious device they were able to record all varieties of such curves experimentally produced as the result of abnormal combinations of the dextrocardiogram and levocardiogram. Their method consisted in the rhythmic stimulation of the right ventricle after the production of right bundle-branch block. By this means it was possible to superimpose the dextrocardiogram upon the levocardiogram in varying time relations. They summarize their results by stating that "combination complexes in which the dextrocardiogram precedes the levocardiogram by a considerable interval are transitional in outline between the normal complex and the complex of left bundle-branch block." The reverse effect also occurs. "Such complexes are diphasic and have a QRS interval intermediate between the natural QRS interval and the QRS interval of bundle-branch block." Finally, "combination complexes in which the levocardiogram and dextrocardiogram begin at almost the same instant resemble the normal type of complex closely."

It is of considerable interest to apply these important findings to the clinical curves derived from our two patients. It will be recalled that a record has been secured from each patient in which complexes, intermediate in form between the fully developed dextrocardiogram and levocardiogram were inscribed. Fig. 4 demonstrates the transition from right-sided effects to left and finally the resumption of right-sided control. In all the complexes, with the exception of the third to the eighth in this record, the main deflection is directed upward and the QRS time is prolonged above normal. They are also diphasic in form and are taken to indicate defective conduction in the left branch of the bundle and to correspond, therefore, in their early stages to the dextrocardiogram for this patient. The fourth to the seventh are of uniform type; the QRS time is in the extreme upper

limit of normal; the complexes are diphasic, and it is justifiable to assume that they likewise represent in their early stages the levocardiogram of this patient. It would, therefore, seem probable that the formation of the intermediate complexes (the third and the eighth in the record) was the result of a shift in the time relationship of dextrocardiogram and levocardiogram. This supposition implies that these intermediate complexes result from the fact either that there are unequal rates of conduction through each branch—the excitation wave commencing at a single site—or that two centers being active, the resulting excitation waves had a shorter distance to travel on one side than on the other. One ventricle would therefore pass into contraction shortly before the other, assuming that both were equally responsive to the stimulus received.

METHOD

The complexes representative of levocardiogram and dextrocardiogram were accurately measured with a Lucas comparator and redrawn to scale. The second and fifth complexes in Fig. 4 were selected as satisfactory for accurate measurement and these have been plotted in Fig. 10. It is established that when dextrocardiogram and levocardiogram are summated algebraically in their correct time relations a curve identical with the normal complex for the same lead results. Now, in neither of the two clinical cases here described do we know the form of the normal complex but it may safely be assumed that in its early stages it varies but little from that derived by the summated effects of the complexes as plotted. In the attempt to decide on the method of reconstruction so as to arrive at the normal curve, a difficulty arose. Should the right- or the left-sided type take precedence in time and if so by how great an interval? Should the earliest deflection of the string as it commences to trace the Q-wave in the dextrocardiogram be plotted against a similar point as regards the R-wave in the levocardiogram? This was the method employed. Had it been possible to know the form of the normal complex, then by shifting the relative positions of levo- and dextrocardiogram so that their summation was identical with it, then the two component curves could have been plotted accurately in their correct time relationship. It is unlikely, however, that the error in plotting them as described amounts to more than a hundredth of a second.

The curves of levo- and dextrocardiogram were accordingly summated algebraically in various time relations and a number of the resulting complexes are shown in the accompanying diagram (Fig. 11). The complex marked "A" is the result of the algebraical summation of the original complexes in their apparently normal relationship, that is to say, as plotted in Fig. 10. It is evident that as the

right-sided effects are retarded (in the succeeding drawings *B* to *E*, Fig. 11) in their relation to the left, the S-wave becomes progressively steeper and the duration of this deflection gradually lengthens. These theoretical complexes conform to the findings of Wilson and Herrmann quoted above, in that, as the levocardiogram is forced to precede the dextrocardiogram, the resulting complexes are transitional in outline between the normal complex and the complex of *right* bundle-branch block.

An infinite number of these combination complexes is possible. A few were selected at random and compared with the actual examples

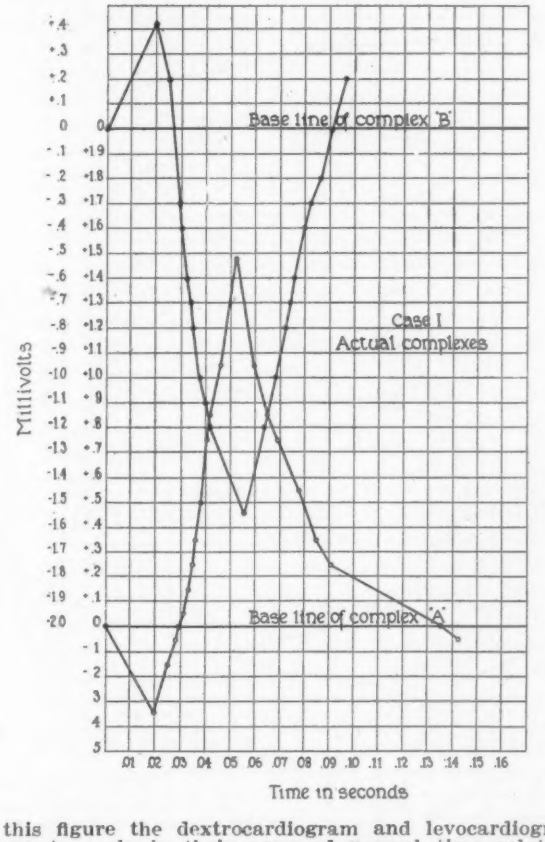

Fig. 10.—In this figure the dextrocardiogram and levocardiogram from Case 1 have been redrawn to scale in their assumed normal time relationship. Complex marked "A" is Complex 2 of Fig. 4 and Complex "B" is Complex 5 of Fig. 4.

of intermediate complexes observed in the same electrocardiogram from which the left- and right-sided effects were plotted (Fig. 4, complexes 3 and 8). It is obvious that the eighth complex in this figure represents a greater disproportion in the time relation of the combined ventricular effects than the third complex, for in the former instance the S-wave in its duration and depth is greater than in the fourth complex. These two transitional complexes were then measured and plotted in the same way as the original (dextro- and levo-

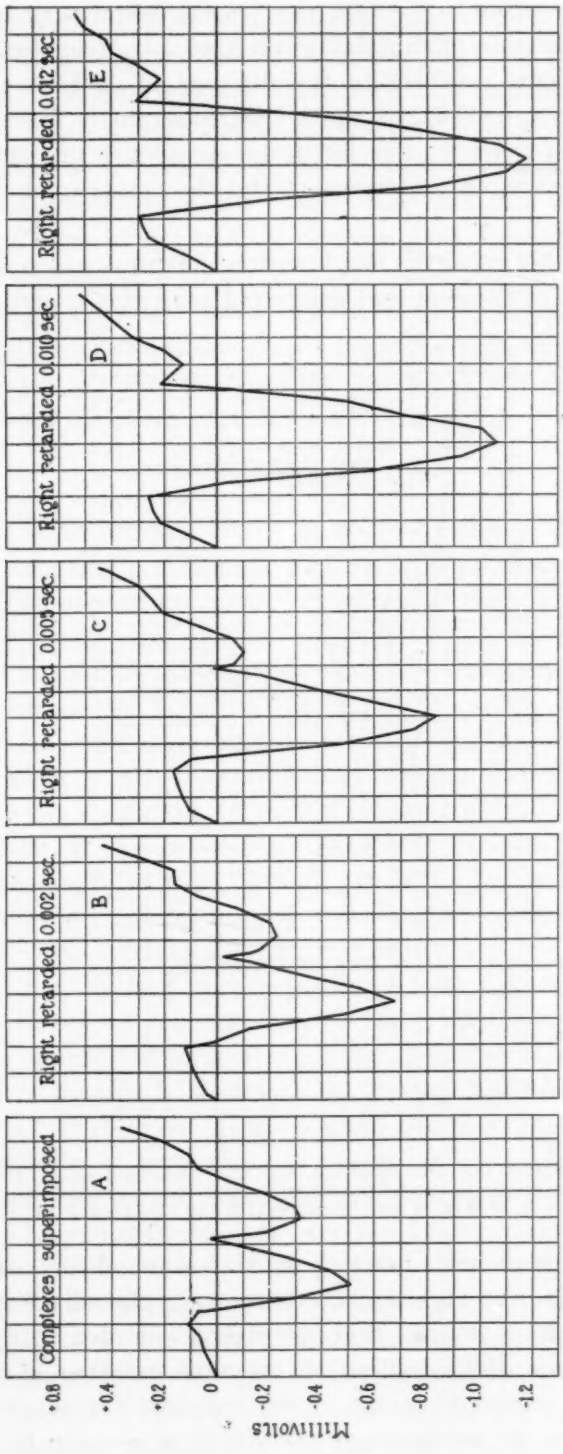

Fig. 11.—Shows the effect in Case 1 of progressive retardation of the dextrocardiogram on the form of the composite curve. The curve marked "A" results from the algebraic summation of the complexes as plotted in Fig. 10.

cardiographic) complexes. For the sake of comparison each was plotted against the theoretical transitional complex to which it bore a superficial resemblance.

FINDINGS

By this method of trial and error it was found that the eighth complex in Fig. 4 was virtually identical in its early time phases with a theoretical complex in which the right-sided effects were retarded 0.012 second. The diagram (Fig. 12) shows the two complexes,—the

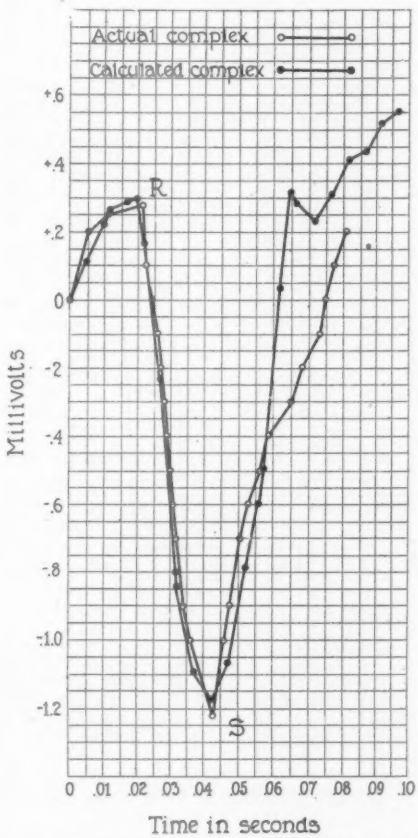

Fig. 12.—"The actual complex" in this diagram is the eighth complex of Fig. 4. The calculated complex is that marked "E" in Fig. 11. They are virtually identical in form in their early time phases.

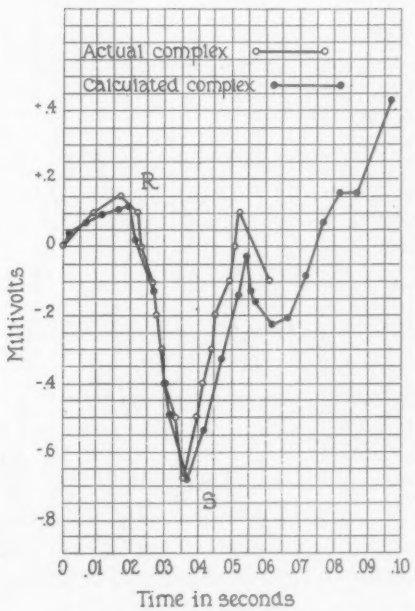

Fig. 13.—"The actual complex" is the first transitional complex in Fig. 4 (Complex 3). The calculated complex is recharted from Fig. 11 "B."

actual and the calculated,—plotted together. In their initial phases they are of virtually identical outline. Such a remarkable similarity must be more than a coincidence. After an interval of 0.043 second the resemblance is less striking and by the time 0.058 second is reached the curves begin to diverge widely. This is not unexpected, for after a time interval of about 0.045 second is reached the right- or left-sided curves no longer represent pure levocardiogram or dextrocar-

diogram. Lewis[18] found that in the dog the composite curve of right- and left-sided effects began to diverge from the normal of the same lead at a value between 0.0350 and 0.0400 second. It may be concluded that the actual complex is to all intents and purposes a duplicate of the theoretical complex resulting from a retardation of the dextrocardiogram by 0.012 second.

In a similar manner it was found that in selecting a theoretical complex to compare with the actual transitional complex, marked No. 3 in Fig. 4, the best match was obtained by a calculated curve in which

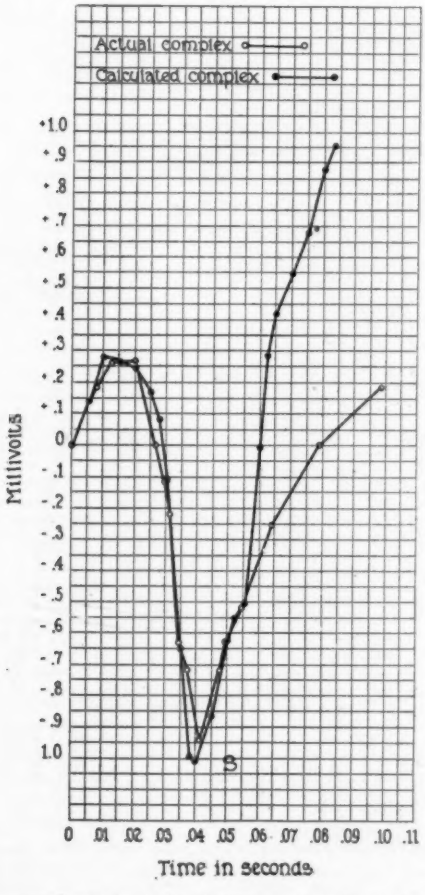

Fig. 14.—"The actual complex" in this diagram is No. 5 in Fig. 7. The calculated curve is derived from retardation of the dextrocardiogram by 0.010 second.

the dextrocardiogram was retarded by 0.002 second. The two, actual and theoretical, are shown in Fig. 13. Up to 0.037 second the similarity between the two is very striking, but after this point is reached the curves begin to diverge.

Similar methods were employed in the analysis of the transitional complexes recorded in Case 2. These are shown in Fig. 7, Lead III, in which the third, fourth, and fifth complexes are frankly interme-

diate in form between the dextrocardiogram and levocardiogram for this patient. It may be pointed out here that these complexes are not diphasic in this patient, that is to say, in the same figure it is seen that the T-wave remains positive throughout, whatever direction the main ventricular deflection immediately preceding it may take. It does, however, change somewhat in form, being of greater amplitude and more sharply pointed with increasing predominance of the S-wave.

From analogy with Case 1 it appears that the fifth complex of Fig. 7 results from the summation of right- and left-sided effects placed relative to each other in such a manner that the dextrocardiogram was

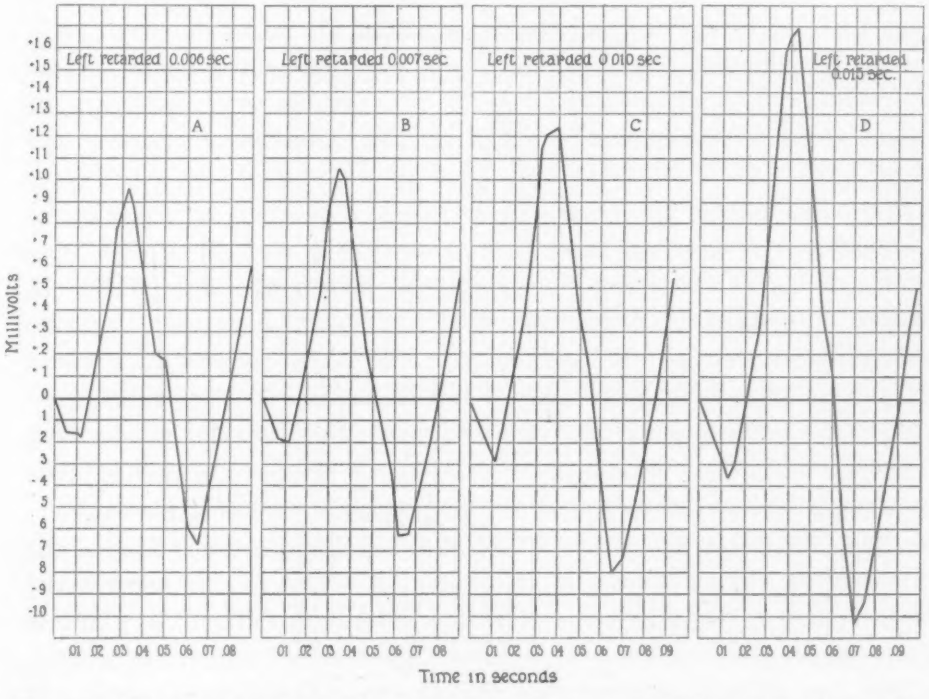

Fig. 15.—This diagram shows the effect of progressive retardation of the levocardiogram in Case 2.

retarded. By trial and error it is found that very close agreement with the actual complex is reached when the right-sided effects are retarded by 0.010 second. The actual complex redrawn from the electrocardiogram and the theoretical complex calculated in the manner described are displayed in Fig. 14. Divergence between the two commences after a time interval of approximately 0.038 second and becomes extreme after 0.055 second.

From the foregoing findings it will be appreciated that the third complex in the same figure (Fig. 7) will result from a relative retardation of the levocardiogram. The effect of progressively retarding the left-sided effects is shown in Fig. 15. It is found that the best fit, be-

tween the actual and the calculated complexes, is obtained when the levocardiogram in the theoretical curve is retarded by 0.007 second. The two complexes are demonstrated in Fig. 16. In this instance the similarity is not so close, the calculated curve being shifted slightly to the left. It may be assumed that the curves begin to diverge at a point 0.035 second after their commencement. At all events divergence becomes quite marked after a time interval of 0.052 second.

In the course of the transition from right- to left-sided effects there is one complex which in itself is intermediate in form between the two

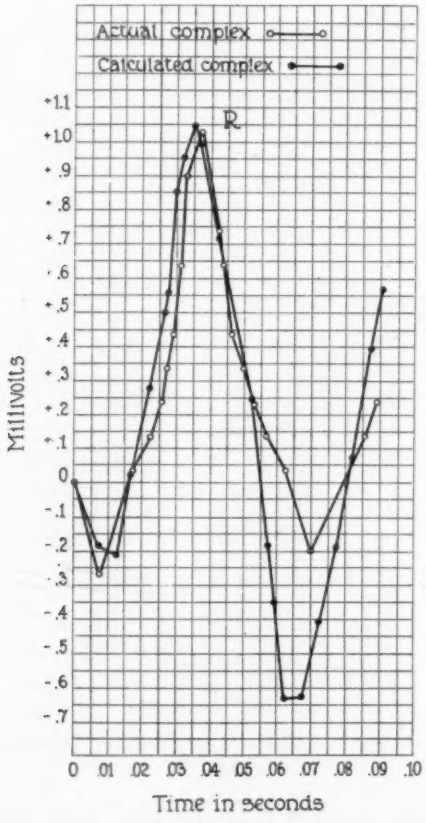

Fig. 16.—"The actual complex" in this diagram is redrawn from Complex 3, Fig. 7. The calculated curve is derived from a retardation of the levocardiogram by 0.007 second. It is redrawn from Complex B in Fig. 15.

just considered. This is No. 4 in the same record (Fig. 7). Accurate measurement of the QRS group is not possible in this instance on account of the distortion of the initial deflection by the presence of a P-wave falling at the same instant. In general then, it may be said that a complex, the result of the summation of dextro- and levocardiogram, in their normal time relations, yields a curve which appears to be very closely similar in amplitude for a given time interval.

The findings in this patient may be summarized by saying that the three complexes (Fig. 7, Nos. 3, 4, and 5) reveal a gradual loss of control by the right ventricle. The first two complexes are the result of a relative lag in the development of the influence of the left side of the heart. In the interval between the second and third complexes the disproportion between the two sides is less marked and when this composite curve is written there is a difference in time relationship between dextro- and levocardiogram of approximately 0.007 second. When the fourth complex is recorded the difference has been neutralized by the recovery of the left side, both elements being recorded in their correct time relationship. This state of affairs is, however, only transient, for in the next complex the left-sided effects have advanced by 0.010 second. The right side has now the weaker influence. A further delay on the right side is responsible for the last complex. In Case 1, there are two transitions recorded in Fig. 4, the left-sided effects being maintained at a constant value for four cycles (Nos. 4 to 7). The transitional complex occurring during the change from predominant right-sided to left effects results from a relative lag in the dextrocardiogram of 0.002 second. The other complex (No. 8) occurring before the right side had recovered completely from its temporary depression, represents a further delay in the development of the dextrocardiogram amounting to 0.012 second; that is to say, the left side has more influence on the form of the composite picture in this transitional complex than it had in the formation of the first transitional complex (No. 3).

There are several factors which are known to influence the form of the initial ventricular deflections and Lewis[19] has arranged them in three groups: (a) the lie of the heart in the chest, (b) the relative weights of the right and left ventricular muscle mass, (c) conduction defects in the bundle branches. In our cases it is possible to disregard the influence of the first two possibilities because they do not apply. We have, therefore, confined our consideration to the nature of conduction in the bundle-branches.

For the sake of comparison with our cases it is instructive to recall the varieties of heart-block which affect the main trunk of the bundle of His. In this situation block may be complete, resulting in auriculoventricular dissociation, or it may be partial. In the bundle-branches complete block is well known, partial is less common. There are various grades of partial block of the main stem commencing with simple prolongation of conduction time. This also has its counterpart in lesions of the branches. A more severe degree of block of the main stem is indicated by the phenomenon of "dropped beats." Wilson and Herrmann[1] point out that a similar defect in a bundle-branch should

lead to a succession of complexes showing (a) a gradual prolongation of the QRS interval until a complex characteristic of complete bundle-branch block is formed. This should immediately be succeeded by decrease in QRS time and a complex of relatively normal outline; or (b) an alternation in the duration of the QRS interval, the wider indicating complete branch block, the other impaired conduction. Clinical curves corresponding to this description, if they do occur, must be very rare. One explanation of Fig. 7 might be derived from such considerations. It is suggested that such a succession of complexes might represent the onset of partial bundle-branch block in one branch with simultaneous recovery of conduction in the other branch. This is the original idea proposed by Cohn.[5] In Fig. 4, the more prominent deflections are in the main characteristic of a branch defect. The first transitional complex (No. 3) might be regarded as occurring during the recovery of the left branch defect and the onset of the right defect; the other (No. 8) during the recovery of this defect and the development of a left-sided lesion. This explanation does not seem entirely satisfactory. It would seem strange indeed that the functional powers of the branches should bear such a reversed relationship one to the other. It is equally difficult to discover why conduction should be more nearly perfect through one branch than the other, though partial defect in conduction in itself would be sufficient to account for the delayed appearance of dextrocardiogram or levocardiogram. As probable an explanation as this would be the converse one, that the conduction rate was now and then accelerated through one branch relative to the other. These possibilities assume a lesion of the main stem with a single center of impulse production immediately below. It is difficult to reconcile the relatively frequent occurrence of complete heart-block due to a lesion of the main stem with the rarity of transitional complexes.

The more probable explanation, based on the experimental findings of Wilson and Herrmann, is that the transitional complexes are due to the interference of two rhythmic centers, one on either side of the heart. This theory assumes the presence of a bilateral bundle lesion, not necessarily of an organic nature, with rhythmic centers immediately below the defects. In this case, the simultaneous discharge of impulses from each center will result in a composite complex of normal outline. By a disturbance of this time relationship the center of impulse production in advance of the other assumes control and the resulting complexes are of the form associated with a preponderance of right- or left-sided effects as the case may be. Transitional complexes may then be attributed to the asynchronous discharge of impulses from each side of the heart. When the time difference between the two centers is small or absent then complexes of virtually

normal form are recorded. As the difference increases the deflections by their form will suggest partial bundle-branch block. A further increase might produce complexes of a diphasic nature, similar to those recorded by Stenström[13] and resembling the theoretical curve marked *D* in Fig. 15, or complexes might be formed more closely comparable to those of complete bundle-block of a single branch. Gradual transitions in form occur when a change in the time relations of the right and left centers of impulse production takes place. The difference in the two theories consists in this: in the first the defect is in unequal conduction, stimuli being developed at a single center; in the second the defect is in stimulus production and not in conduction, each ventricle having its own mechanism. The second seems to us the more credible possibility and seems, therefore, to be an adequate explanation for the phenomena which were observed in these two patients.

The disorder was observed to occur spontaneously when the ventricles were beating slowly. In Case 2 it was not possible to reproduce it by vagal stimulation or paralysis. Adrenalin in the small dose employed likewise failed. This observation is contrary to the findings of de Graff and Weiss.[14] The exhibition of digitan (1.10 gm. in 12 hours) sufficient to induce slight intoxication and to decrease the amplitude of the T-wave, had no effect on the idioventricular mechanism or on the form of the initial deflections. In Case 1 transitional complexes were observed after digitan, 1.0 gm., had been administered. It is not possible to conclude that the drug was responsible for the phenomenon. One patient suffered from congestive failure with Cheyne-Stokes respiration when the disorder was detected; the other was well compensated and in fairly good health. It is not possible to advance a cause for the onset of the malady.

SUMMARY

1. Two cases of complete heart-block are described. Both showed defective bundle-branch conduction, with gradual transitions in the form of the ventricular complex.

2. The curves have a remarkable similarity to those described by Wilson and Herrmann after the experimental production of bilateral bundle-branch block.

3. By the algebraic summation of levocardiogram and dextrocardiogram in varying time relations one to the other, it was found possible to reproduce the transitional complexes for each patient. In this manner the relative amount of delay in the development of levocardiogram or dextrocardiogram was calculated for each strikingly aberrant complex.

4. The phenomenon is briefly discussed and it is concluded that the most likely explanation consists in a change in leadership of the predominant pacemaker from one side of the heart to the other.

5. Various procedures, such as vagal stimulation and paralysis and the administration of adrenalin and digitalis, failed to reproduce the phenomenon in one case which was observed to occur spontaneously.

6. The postmortem findings are described in one case. Examination of the heart showed that the conducting tract was in a sclerosed state without definite interruption of its continuity.

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THE CLINICAL RECOGNITION OF PAROXYSMAL VENTRICULAR TACHYCARDIA*

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IT HAS generally been considered by physicians, even by those who are especially interested in heart disease, that the bedside diagnosis of ventricular tachycardia is difficult or impossible to make. It has been conceded that electrocardiographic tracings are the only means available for such a diagnosis. The difficulty, of course, has been the differentiation of this kind of tachycardia from the more common paroxysmal auricular tachycardia. This brief note intends to mention a few simple clinical points which have made it possible to make the correct diagnosis of paroxysmal ventricular tachycardia at the bedside.

Before discussing the methods of diagnosis, it seems proper to take up the consideration of the importance of recognizing this condition. It is quite well known that paroxysmal auricular tachycardia is generally associated with no organic heart disease and that in many such cases it is a matter of no great concern whether an exact diagnosis is made or not, for the attacks are apt to end spontaneously and do no harm. On occasions this is not true, and direct treatment to end such an attack is of great importance and, rarely, may be life saving. Paroxysmal ventricular tachycardia, on the other hand, is generally but not always associated with grave heart disease, in most instances with disease of the coronary arteries. It occasionally becomes an important complication of an acute attack of coronary thrombosis.[1] Although under these circumstances the attack is apt to be transient, lasting a few hours and thereby producing no particular problem in therapy, it may be persistent and prove fatal. The proper recognition and institution of therapy may therefore be a matter of great importance. Furthermore, apart from the question of therapy, the striking difference in prognostic significance between paroxysmal auricular tachycardia and ventricular tachycardia makes it distinctly worth while to have some methods available for bedside diagnosis for those patients who are not at hospitals where electrocardiograms could otherwise be taken.

A short while ago attention was called[2] to the fact that in paroxysmal ventricular tachycardia, although the heart rhythm is essentially regular, on careful auscultation distinct irregularities could be detected. (Fig. 1.) This is in striking contrast to paroxysmal auricular

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tachycardia in which the rhythm of the heart is absolutely regular.[3] A further point that differentiates the two disorders is that, whereas in the latter the sounds have a constantly similar character, in the

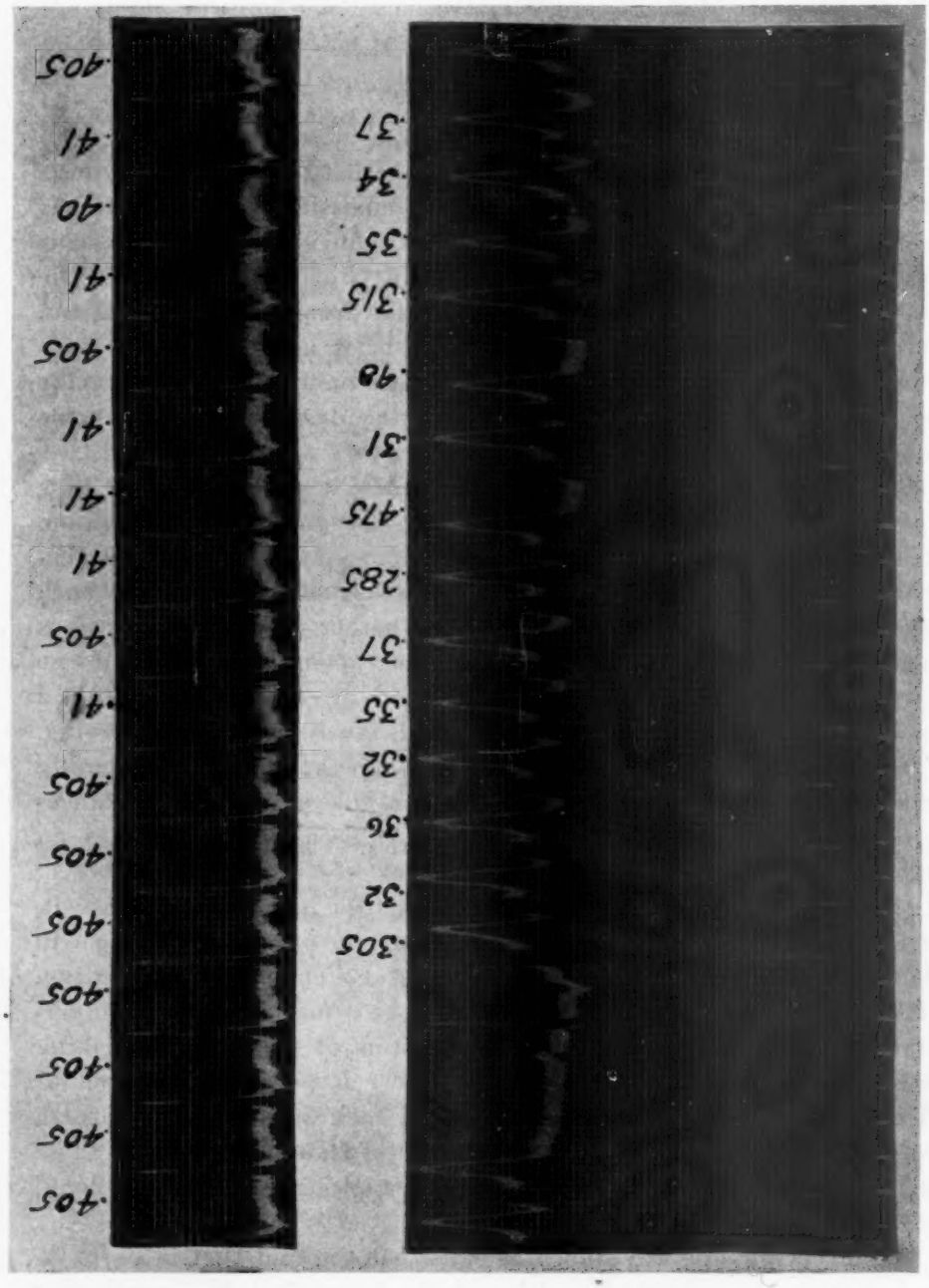

Fig. 1.—Upper tracing shows paroxysmal auricular tachycardia; lower tracing shows paroxysmal ventricular tachycardia, occurring in the same patient. The numbers indicate the length in seconds of the consecutive beats. Note the absolute regularity of the former and the distinct irregularities of the latter.

former the quality and intensity of the first sound heard at the apex is apt to vary with occasional heart cycles. The heart sounds for periods of several seconds may be identical, when suddenly either a click-

ing sound is heard, a muffling, or an accentuation of the first sound takes place. This is not unlike the auscultatory findings in complete heart-block, for here also the quality of the first sound may change in different cycles. The reason for this phenomenon is probably identical in the two conditions. It is due, I think, to the varying relations between the auricular contraction and the ventricular contraction. In paroxysmal ventricular tachycardia the auricles either may be contracting independently or, as in some cases, may be responding to reversed impulses from the ventricle. In either case, the particular auricular systole may occur simultaneously with the ventricular beat, just before or just after it, or may be separated from it by a greater interval. It seems reasonable to suppose that the variations in the quality of the first heart sound can depend upon this relationship and that the sudden accentuation or clicking quality of the heart sounds that one hears is the result of auricular and ventricular systoles occurring at about the same time. Besides these two auscultatory features of paroxysmal ventricular tachycardia, another distinguishing point is the failure to produce any effect upon the tachycardia either by direct vagal pressure or by pressure on the eyeballs. These latter procedures, as is well known, frequently inhibit auricular tachycardia.

The above simple clinical points can be applied at the bedside and have proved distinctly valuable for making the diagnosis of paroxysmal ventricular tachycardia in three instances which have recently been observed. In each case the diagnosis was proved to be correct by electrocardiographic studies. In one of these cases a house officer in the hospital who had never previously seen this condition made the correct diagnosis by using the above criteria.

SUMMARY

There are clinical criteria that enable one to make a bedside diagnosis of paroxysmal ventricular tachycardia. These are slight irregularities in the rapid heart rhythm which otherwise appears quite regular, a changing quality and intensity of the first heart sound as heard at the apex, and the failure to slow the heart by vagal stimulation. This condition previously has been considered unrecognizable except by the use of electrocardiograms. There are instances where the differentiation between this condition and paroxysmal auricular tachycardia is of great importance.

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THE EFFECT OF SODIUM SALICYLATE ON THE NORMAL HUMAN ELECTROCARDIOGRAM*

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WITHIN recent years the electrocardiograph has been used a great deal in the study of the effect of rheumatic fever on the heart muscle,[1, 2, 3, 4, 5] and by this method it has been shown that it is frequently possible to detect evidence of myocardial damage long before such damage can be recognized clinically. Some clinicians[6] have even gauged prognosis with the aid of the electrocardiograph.

In view of the almost universal use of salicylate during rheumatic fever the question has been raised as to whether some of the electrocardiographic changes found in that disease might not be due to the drug rather than to the disease itself. The following study, therefore, has been undertaken to ascertain the effects of the salicylates on the electrocardiogram of normal hearts. Before entering in detail upon the method pursued it will be well to review the electrocardiographic changes recorded in rheumatic fever.

Prolongation of the P-R interval, from a mere depression of conduction that is barely noticeable in the electrocardiogram to dropped beats; partial and even complete heart-block; alterations in the heart rhythm, as for example, sinus arrhythmia, sino-auricular block, nodal rhythm, premature beats, paroxysmal tachycardia, auricular fibrillation and flutter; and finally changes in the contour of the QRS group and the S-T transition interval;—all these have been noted in acute rheumatic fever. Using these criteria, Rothschild, Sacks and Libman[6] found the heart involved in 61 out of 65 cases of rheumatic fever. It is believed that the changes in the S-T interval, i.e., the rise (more rarely the fall) of the R-T or S-T segment directly from the last stroke of the R- or S-wave, respectively, without the usual S-T isoelectric level, is the most common change in rheumatic fever and for this reason particular attention has been paid to this interval.

PLAN OF STUDY

In this study the plan followed was to give sodium salicylate to normal human controls and to watch for the above mentioned changes in the electrocardiogram. Hanzlik[7] states the full therapeutic dose of sodium salicylate to be 15 grams, i.e., 225 grains. In normal subjects this is excreted in about seventy-eight hours. The toxic clinical dose (i.e., until gastric and auditory disturbances supervene)

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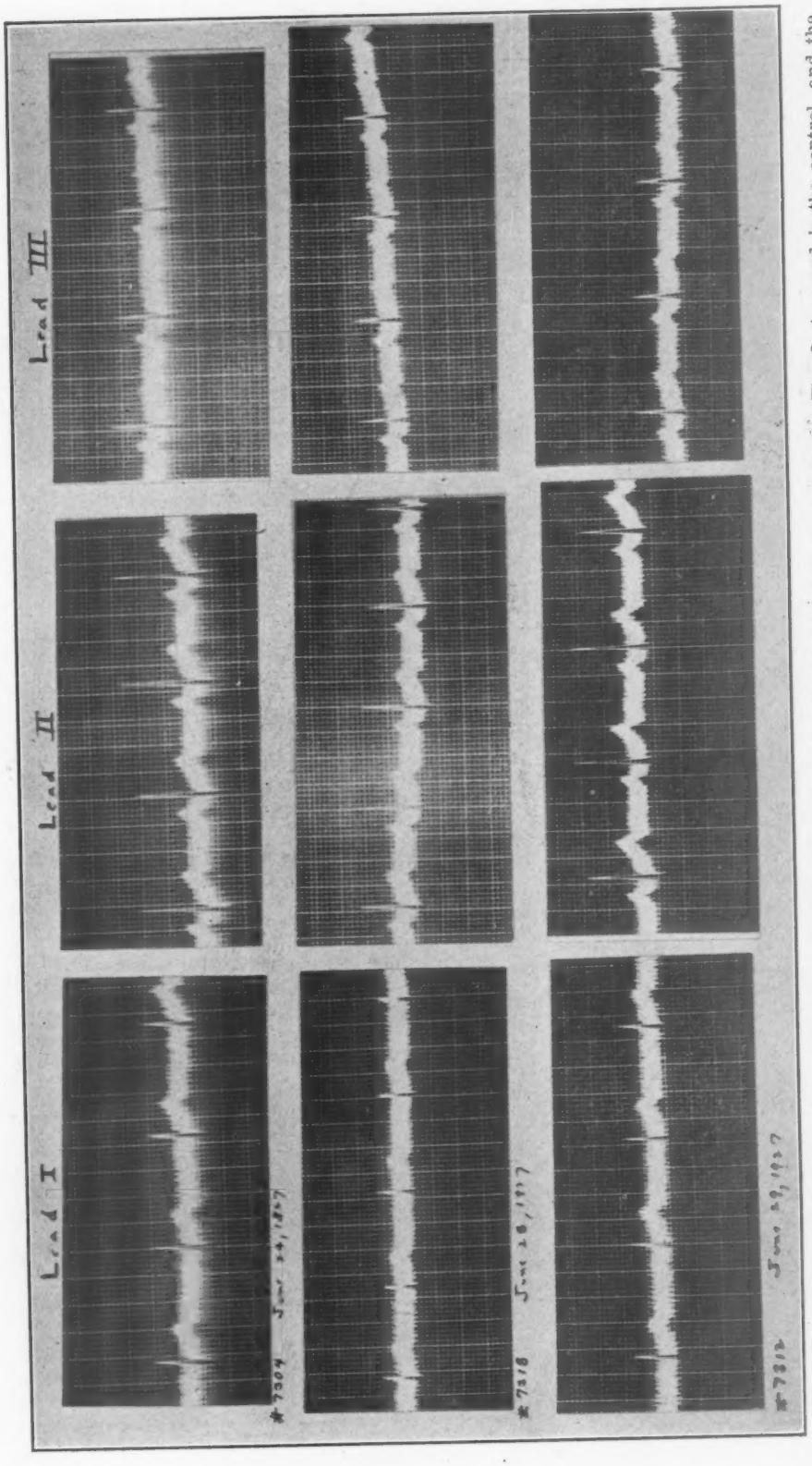

Fig. 1.—(Case 1.) Leads I, II, III. Patient received 840 grains of sodium salicylate in 4-5 days. The first record is the control, and the third is the last record immediately after a total of 840 grains of sodium salicylate were ingested. (See chart.)

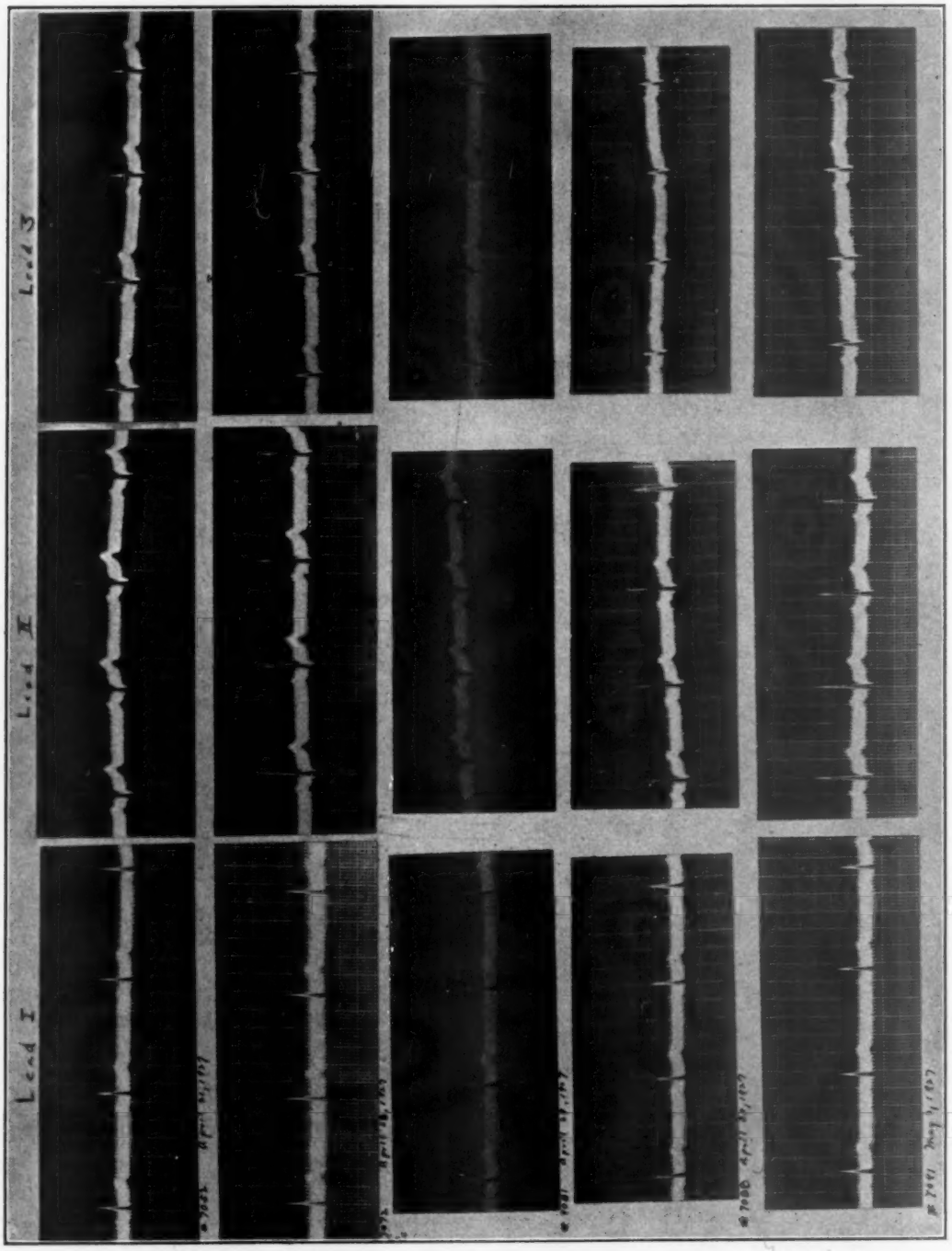

Fig. 2.—(Case 4.) Leads I, II, III. Patient received 720 grains of sodium salicylate in 5-6 days. First record is the control. (See chart.)

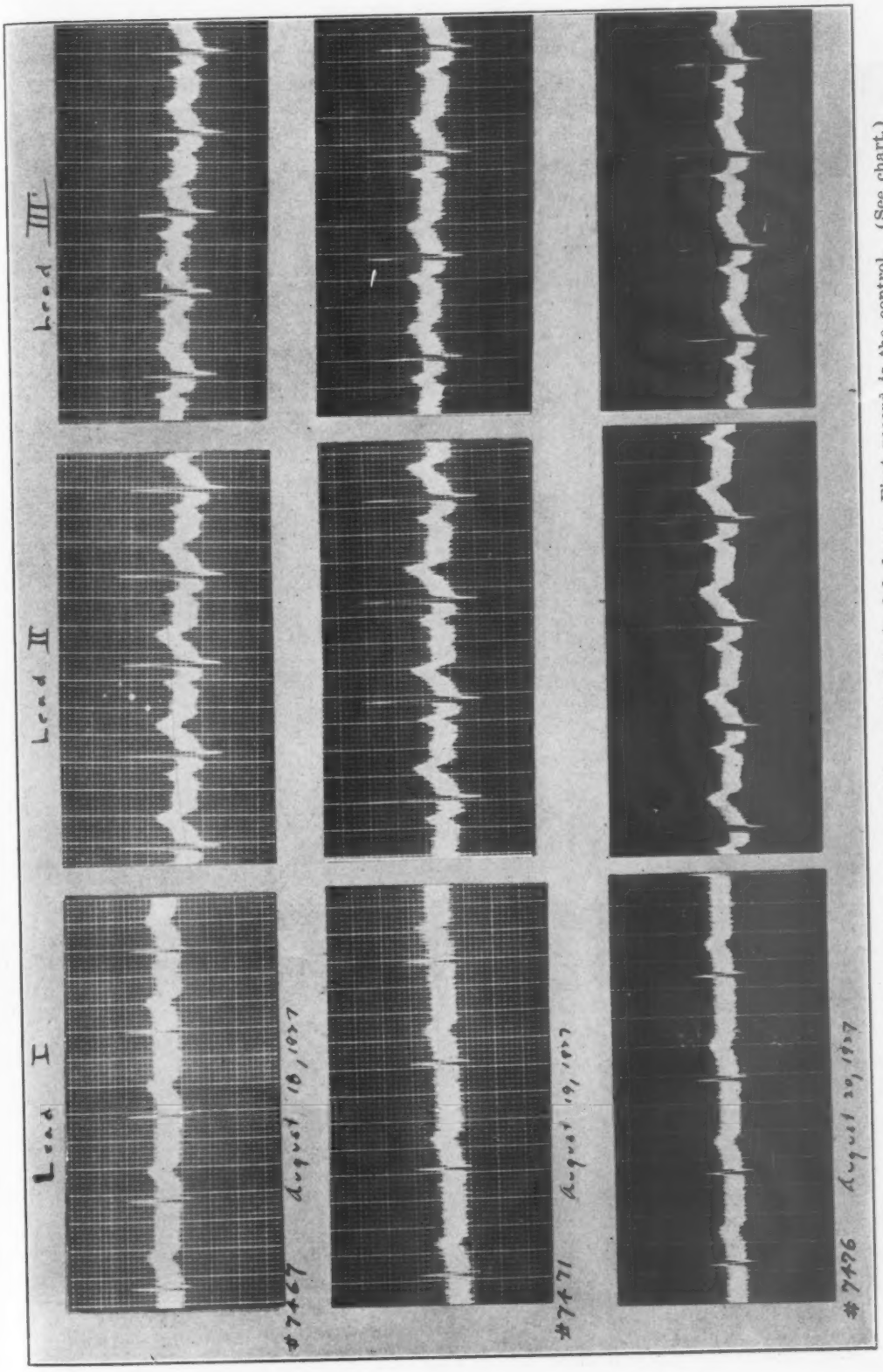

Fig. 3.—(Case 6.) Patient received 360 grains of sodium salicylate in 2-3 days. First record is the control. (See chart.)

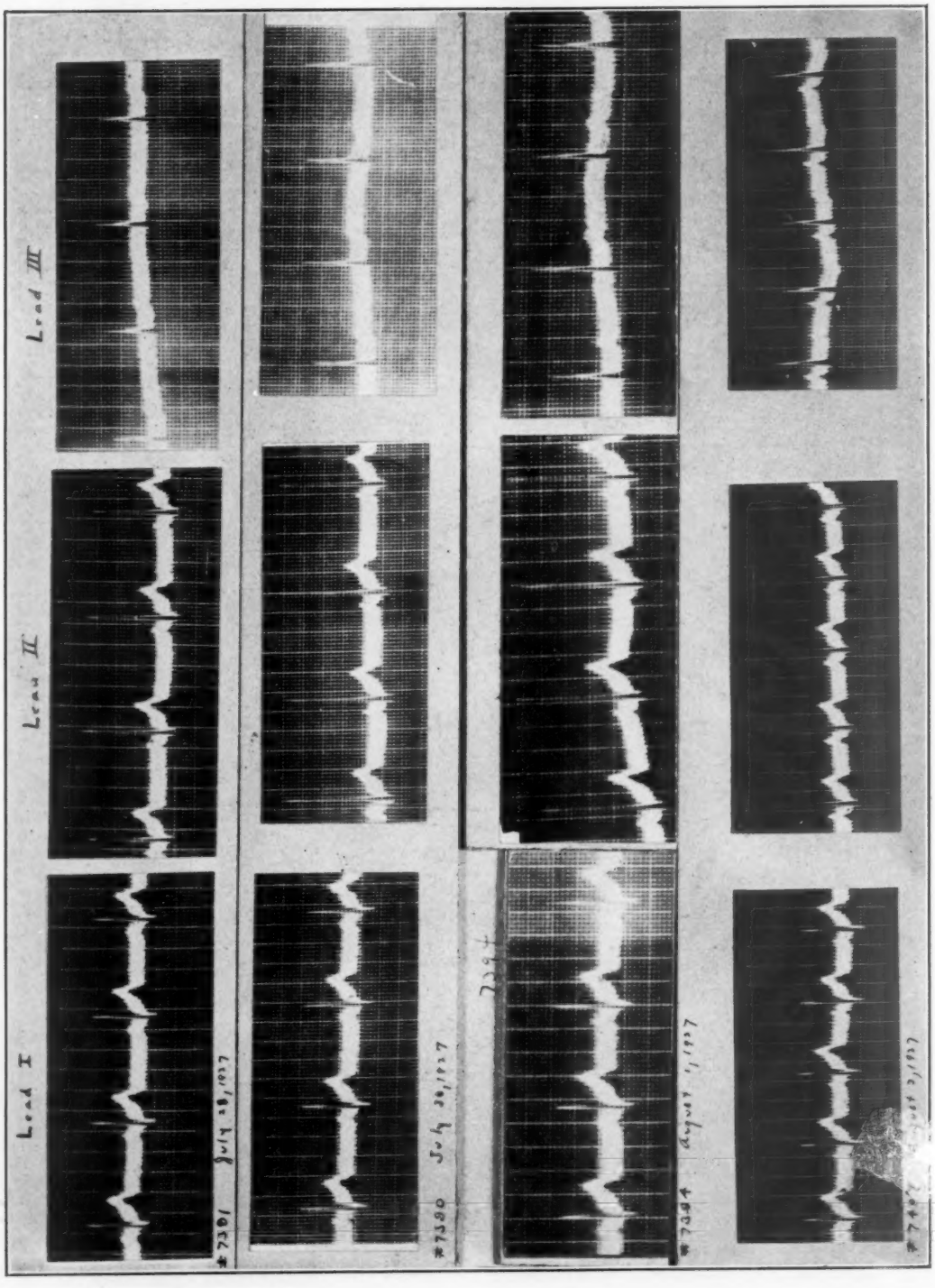

Fig. 4.—(Case 11.) Patient received 600 grains sodium salicylate in five days. First record is the control. (See chart.)

is recorded as from 135 to 200 grains. Females require 80 per cent of the quantity required by men. Deafness, ringing and buzzing in the ears, headache, nausea and vomiting, and sometimes diarrhea were accepted as indications for cessation of the medication. The method

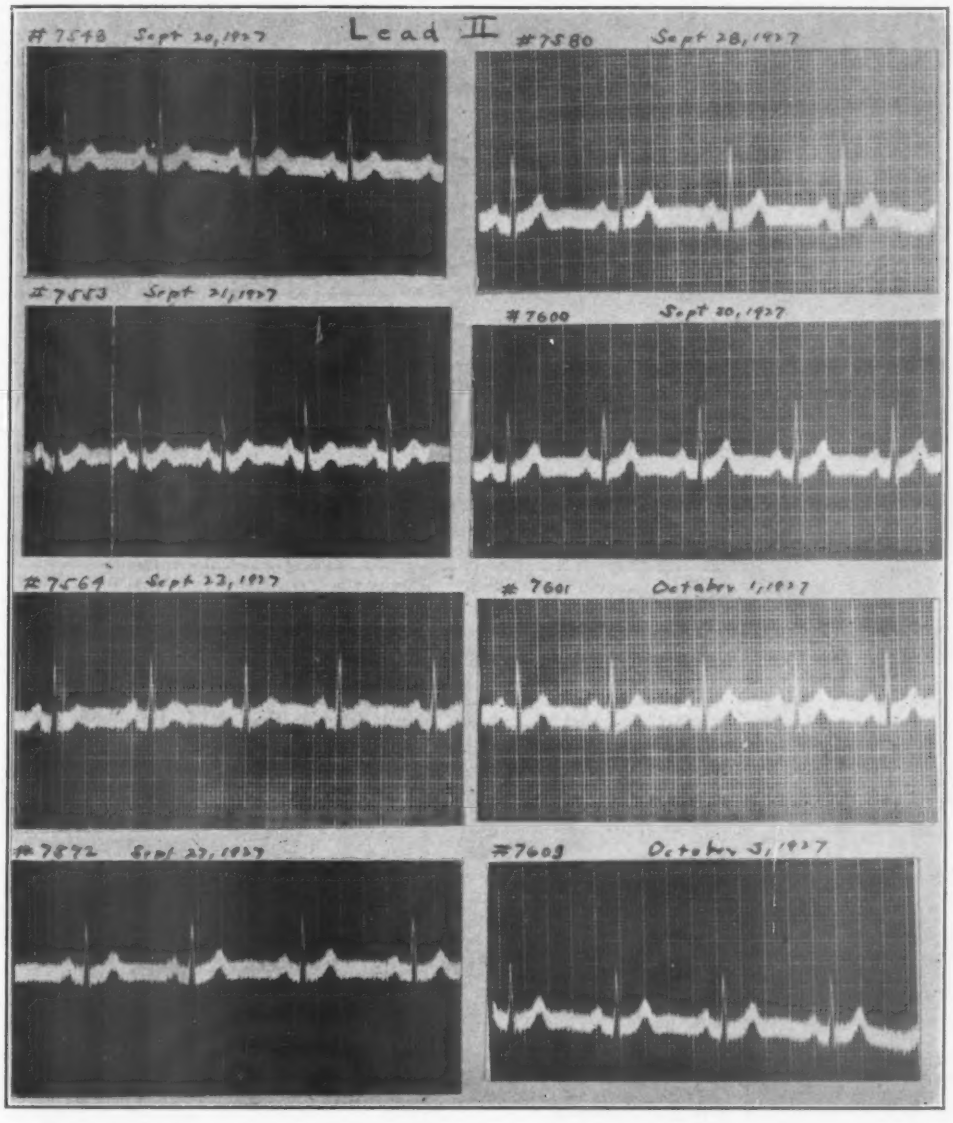

Fig. 5.—(Case 13.) Lead II only. Patient received 1680 grains sodium salicylate in 13 days. First record is the control and the following were taken in the next 13 days. (See chart.)

of administration was twofold, oral and rectal; usually from 60 to 120 grains were given daily by mouth and 120 grains by rectum.

The cases were chosen from the First Medical Service of Dr. L. A. Conner at New York Hospital. As the table shows, they were men and women with normal hearts and lungs, with normal blood pressure,

TABLE I

Case	Age	Weight (Pounds)	Nationality	Time in Hospital	Diagnosis	Condition on Discharge	Symptoms	Physical Examination	B. P.	Laboratory Tests
1 No. 273789	35	130	Spanish	10 Days (6/21/27 to 6/30/27)	Neurasthenia	Improved	Dizzy spells, choking sensation in throat	Negative	112/70	Ewald Test negative, X-Ray gastro-intestinal tract, negative
2 No. 274772	52		French	7 Days (8/17/27 to 8/23/27)	Atony of Stomach Constipation	Improved	Weakness, indigestion, nervousness, eructation	Hernia, right rectus muscle	130/75	X-Ray chest negative. X-Ray gastro-intestinal tract showed a hypotonic stomach
3 No. 273549	49	131	American	33 Days (6/7/27 to 7/10/27	Tuberculosis of Pleura	Improved	Pain in right side	Negative	102/68	X-Ray chest showed chronic fibroid tuberculosis
4 No. 272624	49	145	Haitian	14 Days (4/20/27 to 5/3/27)	Post - operative adhesions	Improved	Pain in epigastrium	Negative		X-Ray chest, slight emphysema X-Ray gastro-intestinal tract showed adhesions around duodenum.
5 No. 273833	31	116	Russian	14 Days (6/22/27 to 7/6/27)	Duodenal ulcer	Improved	Pain in epigastrium	Negative	108/64	Post-pyloric ulcer seen by X-Ray
6 No. 274773	19		American	4 Days (8/17/27 to 8/20/27)	Acute Fibrinous Pleurisy	Cured	Pain in region of left scapula	Negative	110/60	X-Ray chest showed slight congestion in both upper lobes
7 No. 274342	33	103	American	7 Days (7/21/27 to 7/30/27)	Neurasthenia Bradycardia	Improved	Constipation, eructation, regurgitation	Negative	99/66	Gastro-intestinal X-Ray negative. Chest X-Ray negative
8 No. 274387	71	147	American	6 Days (7/25/27 to 7/30/27)	Right Sciatic Neuritis, (Traumatic)	Improved	Pain in right leg	Negative, except local condition	130/80 116/70	
9 No. 274375	38	112	Austrian	6 Days (7/25/27 to 7/30/27)	Neurasthenia	Improved	Pain in stomach	Emphysematous chest	110/80	X-Ray chest showed emphysema. Gastro-intestinal X-Ray negative
10 No. 272627	46	154	Haitian	13 Days (4/20/27 to 5/3/27)	Chronic Cholecystitis	Improved	Pain in epigastrium	Negative		Gastro-intestinal X-Ray showed spasm of of pyloris and antrum.
11 No. 274410	24	118	Filipino	7 Days (7/26/27 to 8/3/27)	Neurasthenia	Improved	Heavy feeling in stomach	Right lobe of prostate hypertrophied	110/70	
12 No. 272817	40	154	Austrian	13 Days (5/2/27 to 5/14/27)	Small abscess right elbow (following Broncho-pneumonia)	Cured	"Grippe"	Slight infection right elbow		X-Ray chest negative
13 No. 275266	42		Italian	18 Days (9/15/27 to 10/3/27)	Low grade benign epidemic Encephalitis	Cured	Hiccough	Negative		X-Ray gastro-intestinal tract, negative

TABLE I

Remarks (Drugs)	Sodium Salicylate*	ELECTROCARDIOGRAM									
		Date	Rhythm	Rate Per Min.	P-R	Height P-Wave	Height QRS. Group	Duration QRS.	Axis Deviation	Height T-Wave	S-T Segment
Small quantity Choral and Luminal		6/24/27	Slight Sinus Arrhythmia	75	0.16 Sec.	2 mm.	10 mm.	0.08 Sec.	None	2.5 mm.	0.28 Sec.
	600 Gr.	6/28/27	"	70	0.16 "	2 "	10 "	0.08 "	"	2.5 "	0.28 "
	840 Gr.	6/29/27	"	77	0.16 "	2 "	9.5 "	0.08 "	"	2.25 "	0.28 "
Paraldehyde on 8/21/27		8/18/27	"	75	0.14 Sec.	2 mm.	12 mm.	0.08 Sec.	"	3.5 mm.	0.28 Sec.
	570 Gr.	8/20/27	"	100	0.14 "	3 "	12 "	0.08 "	"	3.5 "	0.24 "
	780 Gr.	8/22/27	"	75	0.14 "	1.5 "	12 "	0.08 "	"	3 "	0.28 "
		8/23/27	"	80	0.14 "	2 "	12 "	0.08 "	"	3.5 "	0.28 "
Codeine		6/21/27	Normal Sinus Rhythm	75	0.16 Sec.	1 mm.	8–9 mm.	0.08 Sec.	"	2.5 mm.	0.28 Sec.
	225 Gr.	6/11/27	Tachycardia	100	0.16 "	1.5 "	12 "	0.08 "	"	3 "	0.25 "
	495 Gr.	6/14/27	Normal Sinus Rythm	70	0.15 "	1.5 "	10 "	0.08–0.09 "	"	2.5–3 "	0.28 "
	570 Gr.	6/16/27	"	78	0.16 "	1–1.5 "	9 "	0.08 "	"	2.5 "	0.28 "
Slight Amount Codeine		4/21/27	Bradycardia	45–50	0.16 Sec.	1.5 mm.	12 mm.	0.08–0.10Sec.	"	3 mm.	0.30 Sec.
	180 Gr.	4/28/27	"	50–53	0.16 "	1.5 "	11.5 "	"	"	2.5–3 "	0.30 "
	360 Gr.	4/29/27	"	60	0.16-0.17 "	1.5 "	12 "	"	"	2.5–3 "	0.28 "
	525 Gr.	4/30/27	"	54	0.16-0.17 "	1–1.5 "	10–11 "	"	"	2 "	0.28 "
	720 Gr.	5/ 2/27	"	58–60	0.17 "	1. "	11–12 "	"	"	2 "	0.28 "
		6/24/27	Normal Sinus Rhythm	92	0.13 Sec.	2.5 mm.	9 mm.	0.07 Sec.	"	3 mm.	0.26 Sec.
	300 Gr.	6/28/27	"	88	0.13 "	2.5 "	9–10 "	0.07 "	"	3 "	0.26 "
	420 Gr.	6/29/27	"	85	0.13 "	1.5–2 "	7–8 "	0.06 "	"	2 "	0.24 "
		8/18/27	"	81	0.16 Sec.	2 mm.	11 mm.	0.08 Sec.	"	3.5 mm.	0.25 Sec.
	120 Gr.	8/19/27	"	77	0.16 "	2 "	11–12 "	0.08 "	"	3.5–4 "	0.24 "
	360 Gr.	8/20/27	"	80–85	0.17 "	2 "	12 "	0.08 "	"	3.5 "	0.24 "
		7/25/27	"	60–70	0.18 Sec.	2 mm.	10 mm.	0.08 Sec.	"	2.5 mm.	0.28 Sec.
	150 Gr.	7/28/27	"	70	0.18 "	2 "	10 "	0.08 "	"	2 "	0.28 "
	150 Gr.	7/30/27	"	65–70	0.18 "	1.5 "	10–11 "	0.08 "	"	2 "	0.26 "
		7/27/27	"	66–75	0.16 Sec.	1.5–2 mm.	7 mm.	0.08 Sec.	Left	1.5–2 mm.	0.32 Sec.
	450 Gr.	7/29/27	"	75–77	0.16 "	1.5–2 "	7–8 "	0.08 "	"	2 "	0.28 "
		7/26/27	"	82	0.16 Sec.	3 mm.	7–8 mm.	0.08 Sec.	None	5–6 mm.	0.29 Sec.
	210 Gr.	7/28/27	"	72	0.16 "	3 "	7–8 "	0.08 "	"	5–6 "	0.29-0.30 "
	570 Gr.	7/30/27	"	66	0.16 "	3 "	7–8 "	0.08 "	"	5–6 "	0.30 "
		4/28/27	"	75	0.20 Sec.	1 mm.	7–9 mm.	0.08 Sec.	"	1.5 mm.	0.24 Sec.
	180 Gr.	4/29/27	"	85	0.20 "	1 "	8–9 "	0.08 "	"	1.5 "	0.24 "
	270 Gr.	4/30/27	"	70–80	0.20 "	1 "	8 "	0.08 "	"	1 "	0.24 "
	720 Gr.	5/ 2/27	"	80	0.20 "	1 "	7 "	0.08 "	"	1–1.5 "	0.24 "
		7/28/27	Simple Bradycardia	56–60	0.10-0.12 Sec.	1 mm.	17–19 mm.	0.08-0.09 Sec.	"	4 mm.	0.28-0.30 Sec.
	120 Gr.	7/30/27	"	58	0.10-0.12 "	1 "	17–19 "	0.09 "	"	3.5 "	0.28-0.29 "
	360 Gr.	8/ 1/27	"	62	0.12 "	1 "	18–19 "	0.09 "	"	4 "	0.28-0.29 "
	600 Gr.	8/ 3/27	Normal Sinus Rhythm	80	0.13 "	1 "	17 "	0.08 "	"	3 "	0.26 "
		5/12/27	Simple Bradycardia	47	0.12 Sec.	1 mm.	8 mm.	0.08 Sec.	"	3 mm.	0.34-0.36 Sec.
	100 Gr.	5/13/27	"	45	0.12 "	1 "	8 "	0.08 "	"	3 "	0.34 "
	270 Gr.	5/14/27	"	52	0.12 "	1 "	8 "	0.08 "	"	3 "	0.32–0.33 "
		9–20–27	Normal Sinus Rhythm	72	0.18-0.19 Sec.	2–2.5mm.	13 mm.	0 08-0.10 Sec.	"	2.5 mm.	0.25 Sec.
	270 Gr.	9/21/27	"	80	0 18-0.19 "	2.5 "	13 "	" "	"	2.75 "	0.22 "
	480 Gr.	9/23/27	"	72	0.19 "	2.5 "	12–13 "	" "	"	2.5 "	0.24 "
	960 Gr.	9/27/27	"	64–66	0.19 "	2.25 "	13 "	" "	"	3 "	0.265 "
	1080 Gr.	9/28/27	"	62	0.19 "	2 "	13 "	" "	"	3.5 "	0.27 "
	1320 Gr.	9/30/27	"	68–70	0.19 "	2 "	13 "	" "	"	3.5 "	0.25 "
	1440 Gr.	10/1/27	"	72	0.19 "	2 "	12–13 "	" "	"	3 "	0.25 "
	1680 Gr.	10/3/27	"	72	0.19 "	2 "	12 "	" "	"	3.5 "	0.25 "

*The figures in this column indicate the quantity of sodium salicylate taken up to the moment of the next electrocardiogram. The dates of these electrocardiograms are in the following column.

without tachycardia, and without fever. Their ages varied from nineteen to seventy-one years. The diagnosis on discharge was in four cases neurasthenia, and in one case each, atony of the stomach, chronic tuberculosis of the pleura, postoperative peritoneal adhesions, duodenal ulcer, acute fibrinous pleurisy, bradycardia, sciatic neuritis, questionable chronic cholecystitis and abscess of elbow during convalescence from a bronchopneumonia. The subjects were chosen carefully and probably represent as nearly normal individuals as one can find in a medical ward of a large hospital. The total quantity of the drug utilized was in one case 150 grains, otherwise the minimum was 270 grains, and the maximum 1680 grains. The time usually required was from two to five days, and electrocardiograms were taken either every day or every second day. Control electrocardiograms were obtained before any attempt was made to give the medication.

DISCUSSION

Before an analysis of the results is made it is necessary to emphasize two points; first, the electrocardiograms of each individual must always be taken in the same position. The records were usually taken in the sitting position. Change of posture will cause appreciable changes in the electrocardiogram. Secondly, it must not be forgotten that even the normal electrocardiogram varies in slight detail from day to day in the same individual; the rate, for example, may be different, or a sinus respiratory arrhythmia may be present at one time. The amplitude of the waves of the electrocardiogram and the S-T interval will change slightly with these factors. Allowing for these normal variations, the analysis of the electrocardiographic tracings proves conclusively that sodium salicylate has no effect on the electrocardiogram and presumptively no effect on the normal heart muscle. The figures in the table were obtained after making the necessary corrections for standardization, although the illustrations are published without alteration. No curves were accepted that showed overshooting. Table I summarizes briefly the clinical aspects of the cases. In the column headed "Sodium Salicylate" is recorded the amount of that drug given, up to the moment when the next electrocardiogram was taken. In the same table is a résumé of the measurements of the waves and the intervals of the electrocardiograms.

In only two cases (Nos. 2 and 3) was there as great a change in rate as from 75 to 100. Considering that there were more than forty records, taken at different times, this change in rate cannot be ascribed to salicylates. It would occur occasionally in any forty normal electrocardiograms on the same group of individuals. In other words, in people with normal heart rates, therapeutic doses of sodium salicylate produce practically no change in pulse rate. The auriculoventricular conduction time, i.e., the P-R interval, the amplitude of the P-,QRS-,

and T-Waves, and the S-T segment remained practically unchanged. Perhaps most significant of all, the forms of the T-wave and the *contour of the R-T or S-T segments* were absolutely unaltered, as may be seen from the accompanying illustrations. These important findings in conjunction with the P-R measurements, indicate that sodium salicylate has no effect on the normal human electrocardiogram and does not account for any of the electrocardiographic changes noted in rheumatic fever.

SUMMARY

Considering the well-known effect of acute rheumatic fever on the heart muscle, and also considering the fact that the electrocardiographic changes in rheumatic fever have become of considerable importance, it seemed important to study the effect of salicylates on the electrocardiogram of normal persons.

Thirteen individuals, twelve men and one woman, were chosen. These were fairly normal persons who had no disease which affected the heart. Electrocardiographic records were taken before and after the administration of sodium salicylate. The salicylate was given by mouth and by rectum, or when gastric complaints were present, by rectum alone, until signs of salicylism appeared.

In studying these records it is seen that sodium salicylate produced no effect on the pulse rate. The auriculoventricular conduction time, the form and amplitude of the QRS group, and the contour of the R-T or S-T segment were unaltered; the P- and T-waves similarly were not affected. The *electrocardiogram therefore is not changed by sodium salicylate,* and there is no evidence that the drug has any effect on the normal heart muscle.

In rheumatic fever electrocardiographic changes are almost invariably present. As sodium salicylate has been shown to cause no changes in the electrocardiograms of normal persons, the drug cannot be held responsible for the changes which are found in individuals with this disease. The electrocardiographic changes enumerated by various authors in rheumatic fever are not the result of salicylate therapy, but are due to heart muscle disease which is present in spite of the use of the salicylates.

I wish to express my sincere thanks to Dr. L. A. Conner for his kind supervision of this work and for his helpful suggestions.

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THE HEART AFTER SEVERE DIPHTHERIA

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and

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THE most important study dealing with cardiovascular disease is that relating to its etiology, since progress in the future control and prevention of such disease is dependent on greater knowledge of the causes. One of the infections which is known sometimes to involve the heart severely during its course is diphtheria. The literature of recent years abounds in reports of the graphic studies of various cardiac abnormalities during the course of the acute disease. Formerly many clinicians considered diphtheria as sufficient cause for various types of permanent cardiac abnormality. In recent years, with newer methods of study and some changes in interpretation of heart findings, the opinion seems to have become slowly diffused that should an individual recover from the acute infection, even though cardiac involvement occurred, no permanent detectable abnormality of the circulatory mechanism becomes established.

The occasion for our present interest in this subject was the finding by Dr. Edwin A. Place, of the South Department, Boston City Hospital, of one case of high grade heart-block which developed on the third day of diphtheria and became permanent. The patient was a girl, aged two to three years, seen in 1907. There was a rather indefinite story of congenital heart disease which was not demonstrable when first observed. On the third day of diphtheria her pulse suddenly dropped from 120 to 50, and the slow pulse persisted after recovery. Electrocardiographic study in 1916 and 1919 showed complete auriculoventricular block, auricular rate 80-100, ventricular rate 40-50. When last seen, in the spring of 1926, she was feeling perfectly well, but still exhibited complete heart-block, nineteen years after having diphtheria. There is doubt as to the actual causation of this permanent block by the diphtheria, in the absence of other evidence of serious myocardial damage, but this seems to be a case of persistent diphtheritic heart-block. The case was recently reviewed by Sprague and White,[1] in a series of young individuals with heart-block.

Another interesting case in this connection is that of Parkinson,[2] reported in 1915. A young man, aged twenty-two years, developed complete heart-block twenty-three days after the onset of pharyngeal

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diphtheria. This was shown one week later by polygraphic tracings. Three days later, or thirty-three days after the onset, his pulse was found to be absolutely irregular and about 60 per minute. A polygraphic tracing showed the presence of auricular fibrillation. During convalescence the ventricular rate increased to 100 per minute, but the auricular fibrillation persisted, and was present six months after recovery. Parkinson (personal communication) states later that through the patient's mother it was learned that he was passed for India at the beginning of the war (1914-15) and that she had good news of his health in India. It was not known whether the auricular fibrillation had disappeared, or the ventricular rate was such that he had no symptoms and could pass a medical examiner. He remained in active service in India during most of the war; then contracted malaria but recovered, returning to England "a picture of health" in 1919. After six weeks in England he is said to have had a relapse of malaria, leading to double pneumonia and death (in 1919).

In 1904 in a clinical study of 964 cases of diphtheria, White (F. W.) and Smith[3] stated that the great frequency of heart murmurs and a rapid or irregular pulse during the course of the disease and their persistence for a long period of time made it desirable to watch the condition of the heart long after convalescence. White (F. W.),[4] in 1905, reported the subsequent examination of 78 such cases six to twelve months after diphtheria. Only twenty patients showed any abnormality after from two to four months. Six cleared up in from six to eight months. Of the thirteen cases under suspicion when last seen, five had been observed for five months, four for six months, two for eight months, and two for eleven months. The exact findings were somewhat vague as to the criteria considered as evidence of abnormality. White considered the cardiac disturbance usually that of mitral insufficiency with irregular heart action but few symptoms. He concluded that cardiac disturbances often last for from two to six months, and in many cases do not clear up in the first half year, but last much longer; some ultimately recover; "others probably do not."

Schwensen,[5] in reviewing 568 cases of diphtheria, with particular reference to rhythm, reported that he found that forty of the sixty-six patients diagnosed as having "myocarditis" during the diphtheria and reexamined two years after recovery still showed signs of impairment of the heart. He concludes that diphtheria must be considered an important cause of heart failure later in life. Here again, the criteria of determination are not definite, functional disorders seemingly being considered as evidence of organic disease. Again, Schwenson states that in some cases in which reexamination showed pronounced impairment, there had been during the acute illness only doubtful signs of myocarditis, which does not seem in keeping with all of his conclusions.

Evidence of cardiac involvement during diphtheria is often vague. Of course the development of heart-block, auricular fibrillation, gallop rhythm, and circulatory failure is definite enough; the vague terms, irregularity of the pulse (without interpretation or determination of the irregularity), extrasystoles, muffling of the sounds, weak sounds, split sounds, variations in the diastolic pause, and systolic murmurs (without intelligent interpretation), do not convey definite pictures of cardiac abnormality. The entire field is ill-defined, and for this reason alone, it would seem desirable to follow up the after-records of such cases and to determine any permanent effect of diphtheria on the heart.

It was decided by us three years ago to study as many cases of severe diphtheria as possible, at least five years after the disease, and to compare the present findings with those at the time of the illness. With the kind cooperation of Dr. Edwin A. Place, Director of the South Department, Boston City Hospital, 100 patients have been reexamined.

MATERIAL

Of the 100 patients whom we were able to locate, 70 (or 70 per cent) were diagnosed as having severe diphtheria, and 30 (or 30 per cent) moderately severe diphtheria. All cases were proved by culture, and were patients at the South Department, Boston City Hospital, five to eight years prior to reexamination. Of the severe cases, all but seven required 24,000 or more units of diphtheria antitoxin, and the vast majority required 36,000 or more units. They were either diagnosed as having "myocarditis," or gave some evidence of cardiac abnormality, or ran severe toxic courses. Faucial diphtheria often along with laryngeal and occasionally with nasal, was the rule. Sixteen patients required intubation, and nineteen had some form of paralysis. To the moderately severe cases 12,000 to 24,000 units of antitoxin were given, and the disease had a less severe course in general than in the former group, though there were almost as many functional heart findings as in that group. In the two groups there were 42 per cent of males, and 58 per cent of females. Forty-one patients were under five years of age, 43 between five and ten years, 9 between ten and fifteen years, and 7 were above fifteen years.

Six other patients were studied and ruled out, five because of acute rheumatic fever since diphtheria, and one because of a congenital defect, noted at the time of illness.

METHODS OF STUDY

The methods of study to determine whether or not any organic heart disease existed were history-taking, with especial reference to the cardiovascular system, routine physical examination with careful

heart findings, electrocardiographic tracings on all cases, and x-ray examination when there was question of cardiac enlargement.

Especial attention on examination of the heart was paid to heart size, rhythm, and to the interpretation of cardiac murmurs.

RESULTS OF STUDY

History.—No single patient reexamined gave an interval history suggestive of organic heart disease, and there were no symptoms at the time of examination.

Physical Examination.—1. Size: Heart size was rather easily determinable in most cases since there were few adults in the group presenting the common difficulties, such as obesity, emphysema, large breasts, etc. There was a question of slight cardiac enlargement in two patients, but x-ray examination showed the hearts to be well within normal limits.

2. Rhythm.—Two patients exhibited ventricular premature beats occasionally. Fifty-two patients of the group had slight to moderate sinus arrhythmia. None of the patients had gallop rhythm or heart-block, or any type of irregularity other than the above.

3. Murmurs.—Thirty-three of the 100 patients showed some form of systolic murmur; there were no diastolic murmurs. Seventeen of these systolic murmurs were faint, short apical systolic murmurs heard only in the recumbent position and increased by exercise. Thirteen were basal functional systolic murmurs, varying with respiration. Three were fairly loud apical systolic murmurs, disappearing on deep inspiration, not masking the first sound, and not associated with accentuation of the pulmonic second sound. In short, there were heard no murmurs pathognomonic of valvular disease. The murmurs heard would be considered functional and in no sense evidence of endocardial damage.

4. Heart Sounds.—The heart sounds were good in all patients. There were no weak or muffled sounds. There was a split first sound at the apex in one patient. Twenty-five patients exhibited third heart sounds.

5. Blood pressure determinations in all patients were within normal limits.

6. Electrocardiographic Records.—One record showed a questionable auriculoventricular nodal premature beat and ventricular escape. Two records showed slight right axis deviation, postural in origin. No other evidence in any way suggestive of abnormality was found.

7. Roentgenology.—Two patients were studied by means of the x-ray, because of questionable slight cardiac enlargement; the heart size was found to be within limits of normal in both.

SUMMARY

No evidence of organic heart disease was found by history, physical examination, routine electrocardiogram, or x-ray (when needed). There were a number of patients showing functional systolic murmurs, sinus arrhythmia, third heart sounds, and two exhibiting premature beats.

COMPARISON OF FINDINGS

Twelve patients of the severe diphtheria group (70), or 17.1 per cent, were originally diagnosed as having "myocarditis"; of these twelve patients seven had systolic murmurs at the time of the diphtheria, none of which could be considered as being organic systolic murmurs from the description. Four of this group of seven still have functional systolic murmurs. Of the five patients diagnosed as having "myocarditis" without systolic murmurs, two were found on reexamination to have functional systolic murmurs. The diagnosis of myocarditis was based largely on the presence of gallop rhythm (4), split, weak, doubled or muffled sounds (8), and extrasystoles (10). There was no evidence, in reexamining these twelve patients, of any suggestion of abnormality.

Twenty-nine systolic murmurs were described during the acute illness. Twenty-four were called functional or described as such. Two were thought to be indicative of organic disease but disappeared before discharge. Two other supposedly functional murmurs and one questionable apical diastolic murmur were not heard at discharge. The remaining systolic murmur thought to be organic was not heard on our reexamination.

Premature beats were present at the time of the diphtheria in ten patients, but no patient exhibiting this phenomenon during the disease was found to exhibit it afterwards. Two moderately severe cases, without any sign of cardiac damage, showed premature beats on reexamination. Of patients with other irregularities, mention was originally made of only four, two having irregular pulses, and two intermittent pulses. All four patients had normal rhythm on the follow-up examination.

Only two patients were thought to have cardiac enlargement at the time of the illness, and this was not present either upon discharge or upon reexamination.

SUMMARY

1. Two cases suggesting that diphtheria may have an after-effect on the heart are cited.

2. From a study of 100 young people who have had severe (70 per cent) and moderately severe (30 per cent) diphtheria five to eight

years prior to examination, there is no evidence of appreciable chronic effect of diphtheria on the heart.

NOTE.—We wish to express our appreciation to Doctor Edwin A. Place for his cooperation in making this study possible; and to Doctors W. S. Burrage, J. F. Kellogg, S. G. Mudd, and H. B. Sprague for their valuable assistance.

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OBSERVATIONS ON A CASE OF HEART-BLOCK IN ACUTE RHEUMATIC FEVER UNDER TREATMENT WITH DIGITALIS*

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IT IS well recognized that one of the manifestations of the effect of acute rheumatic fever on the heart is damage to the conducting mechanism. Parkinson, Grosse and Gunson[11] found evidence of it in fifteen out of fifty cases, while Cohn and Swift[2] in their study of myocardial involvement in rheumatic fever encountered some change in conduction thirty-one times in thirty-seven cases. Coombs[5] states that changes are sometimes present, but his observations do not show such a high incidence as the other authors reported. In the great majority of cases the effect is transient and is rarely more severe than a prolongation of the P-R interval, although it may proceed to the extent of occasional dropped beats, while Parkinson and his coworkers had three cases in which ventricular automatism was present.

The action of digitalis on the heart has been extensively studied both in animals and in man and full reviews of the subject have been published recently by Cushny[6] and by Robinson.[13] One of the common effects of the administration of digitalis is delayed conduction between the auricle and ventricle. As a rule when the rhythm is governed by the normal pacemaker in the sinoauricular node therapeutic doses of digitalis produce no more than a prolonged P-R interval although in some cases dropped beats may be present. Complete heart-block in man due to the action of digitalis has been described by a few observers only. Hewlett and Barringer[7] described such a case and Cohn[3] also reported one in which he attributed the condition to digitalis. Christian[1] added three cases and Wedd[15] published two cases, while Luten[10] observed it four times in his investigations.

One of the most interesting problems in the study of the action of digitalis on the heart is the relative extent to which a given effect is produced by inhibition and by direct action on the heart muscle. All investigators agree that in the heart with normal rhythm the slighter effects are due to inhibition, but in the case of the more marked effects there is a certain amount of divergence of opinion as to the extent to which direct muscular action plays a part. Cushny[6] believed that heart-block due to direct action is only slowly developed

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and at first may be made more complete by inhibitory action but later becomes independent of it. He considered that the part played by each mechanism varies, but as a rule the muscular element predominates in the later stages, although when the cardioinhibitory mechanism is very sensitive marked effects can be produced by it alone. Wedd[15] confirmed the conclusions to which Cushny had come. Cohn and Fraser[4] in their study found that the administration of atropine caused the conduction time to return practically to its normal condition regardless of the degree of depression which had been present. They also found that the heart rate, when reduced, was often not restored as completely as the conduction. White and Sattler[16] reported that atropine relieved the defective conduction in all the cases which they studied. In most of the cases of complete heart-block due to digitalis which have been described, atropine was not given, but in the two cases reported by Wedd it relieved the condition, while in that of Cohn it was without effect. Ritchie[12] described three cases of digitalis bigeminy in which atropine restored normal rhythm, although in one case premature contractions were not wholly removed. He did not consider the effect was due to an increase in rate as the bigeminy might disappear without any increase in the ventricular rate.

The patient who was the subject of the present investigation suffered from acute rheumatic fever and while under treatment with digitalis developed a marked degree of heart-block which was almost entirely relieved by atropine. During the course of study other interesting observations were made which will be described later.

CLINICAL NOTES

History.—M. G., aged twenty-three years, was admitted to the wards of Prof. G. Lovell Gulland on November 29, 1926, complaining of severe pain in the legs. Her height was 4 ft. 8 in. and her weight 7 st. 11 lb. (109 lb.). She was one of a large family and one sister suffered from rheumatism. Patient had no previous history of rheumatism, but since childhood had suffered frequently from tonsillitis. For many years she had had periodical attacks of severe headache and vomiting. During this time she was unable to retain any food, while in the interval between attacks she suffered from indigestion. For three years she had had dyspnea on exertion, palpitation and occasionally precordial pain. Two weeks before admission patient developed tonsillitis, but continued to work until severe pain in the legs compelled her to remain in bed. This pain was of a sharp, stabbing character and increased in severity. It extended from the hips downward in both legs. It was most severe in the region of the knees although it did not seem to be localized to the joints. There was also slight pain in the left shoulder. A few days before admission patient was seized with severe headache and frequent vomiting, and became very drowsy and restless. At the same time cough developed, and the sputum, which had a thick, greenish appearance, was copious.

Physical Examination.—The temperature on admission was 102.6° F. Patient had a pale, pasty appearance. There was great joint pain on movement of the legs but no swelling of the joints was present. The thyroid gland was slightly en-

larged. The tonsils and nasopharynx were inflamed. The pulse rate was 112 per minute and was regular in rhythm. The blood pressure was 132 mm. systolic and 86 diastolic. The apex beat was not visible and no thrill was present on palpation. The cardiac dullness extended 2.5 cm. to the right of the middle line in the fourth interspace and 10.5 cm. to the left in the fifth interspace. A slight systolic murmur was heard at the apex, and this was propagated towards the axilla for a short distance. The sounds were closed at the other areas, but there was accentuation of the second sound in the pulmonary area. There was a small area of dullness at the right base posteriorly over which harsh breath sounds were heard. The vocal resonance was normal and no râles were present. Patient was examined by the Ear, Nose and Throat Department which reported that there was a slight tendency to atrophic rhinitis and that a central perforation of the right tympanic membrane was present, but there was little pus in the right ear. The physical examination was otherwise negative.

Progress Notes.—Patient rapidly improved after admission, and the temperature fell to normal on the fourth day. It remained normal except on a few occasions when there was a rise of about 1.° The pain in the legs rapidly subsided especially after salicylates were given, and soon became absent. The cough and sputum quickly disappeared. Patient had periodic attacks of severe headache and drowsiness throughout the time she was in the hospital. One of these was particularly severe. It commenced on December 23 and lasted until December 27. During this time the temperature remained between 99° and 100°. The changes which took place in the rate and rhythm of the heart during the time she was under observation are fully discussed below. The size of the heart remained constant, but the systolic murmur in the mitral area became more marked and the pulmonary second sound more accentuated. A systolic murmur developed in the pulmonary area and gradually increased in intensity until when the patient was discharged from the hospital this was louder than the murmur at the apex. Patient was sent to the Convalescent Home and while there developed another severe attack of headache which was accompanied by a discharge from the left ear. This condition rapidly improved under treatment. It seems probable that an infection of the middle ear was responsible for the headache and drowsiness from which she periodically suffered. When finally discharged, patient's only complaint was slight dyspnea on exertion.

MEDICATION

Nov. 30 to Dec. 9	–	Tinct. digitalis, m. x, four times a day.
Dec. 10	–	Sod. salicylate, gr. xx, sod. bicarb., gr. xxx, four times a day.
Jan. 17	–	Tinct. digitalis, 1 drachm.
Jan. 18	–	Tinct. digitalis, half a drachm in the morning and m xv at noon and night.
Jan. 19 to Jan. 31	–	Tinct. digitalis, m. xv t. i. d.
Feb. 1	–	Tinct. digitalis, m. xv, four times a day.
Feb. 2 to Feb. 4	–	Tinct. digitalis, m. xv t. i. d.
Feb. 7	–	Tinct. digitalis, m. xv, daily.

CHANGES IN THE HEART RATE AND RHYTHM

Dec. 6.—On the morning of this date after patient had received four drachms of tinct. digitalis in six days it was noticed that an occasional heartbeat was dropped but the rhythm became regular on the slightest excitement. If one assumes a daily excretion of twenty-two minims of tinct. of digitalis[13] the amount in the system at this time was about two drachms, whereas, according to Eggleston's

formula, the quantity necessary to produce the maximum therapeutic effect in this patient ought to be slightly over four drachms.

An electrocardiogram was taken, but no dropped beats were seen (Fig. 1-*A*). The tracing showed a heart rate of 111 per minute and the P- and T-waves were superimposed, while the P-R interval was 0.28 of a second.

Dec. 7 and 8.—The administration of digitalis was continued and dropped beats became more frequent while they did not disappear so readily on excitement.

Dec. 9.—A record showed a more advanced stage of heart-block (Fig. 1-*B*). The degree of block varied—every third to fifth auricular beat was blocked. The auricular rate was between 95 and 100 while the ventricular rate varied between 86 and 68. Three-two rhythm is illustrated and T is seen to be markedly inverted except where P and T are superimposed when the deflection is positive. Occasional ventricular complexes of abnormal form resembling right ventricular extrasystoles were seen. These invariably followed a dropped beat. Patient at this time had received six and two-thirds drachms of digitalis in ten days. Digitalis was now discontinued.

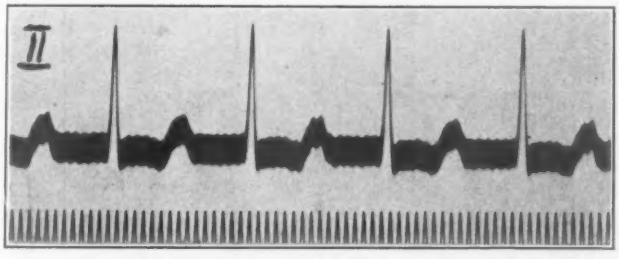

Fig. 1-*A*.—Lead II. Dec. 66. P and T are superimposed. P-R interval is 0.28 of a second. (For full description see text.) In all records time marker is 28.57 vibrations per second. 1 cm.=1 millivolt.

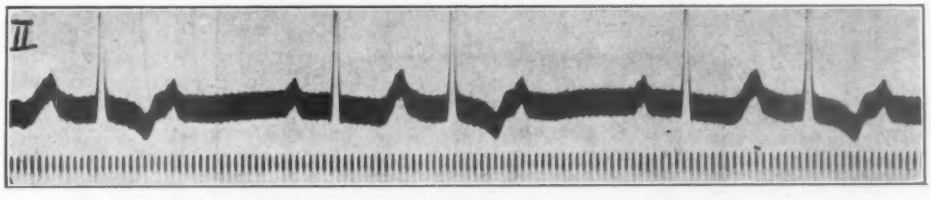

Fig. 1-*B*.—Lead II. Dec. 9. 3-2 rhythm.

Dec. 11.—Many electrocardiograms were taken as it was found that, although the rhythm usually varied between 2-1 and 3-2, from time to time complete dissociation between the auricle and ventricle was present. This usually lasted for a varying number of beats, the maximum seen being seven, and then the heart reverted to its previous rhythm. The ventricular complexes during the dissociation were of similar form to the isolated abnormal ventricular complexes observed on Dec. 9. The auricular rate during complete block was 109 while that of the ventricle was 53. One left ventricular extrasystole was seen.

Dec. 14.—A similar degree of heart-block was still present and periods of complete dissociation were frequent (Fig. 2). During the idioventricular rhythm in Lead I there were two auricular complexes to each ventricular and these appear to bear a relation to one another, but Leads II and III leave no doubt that the auricles and ventricles were beating independently. The auricular rate varied between 95.2 and 101.7 in the different periods of dissociation while the ventricular rate was 50.2 except in Lead III where it was 53.5. The auricular complexes showed two rhythms. The interauricular interval during which ventricular systole

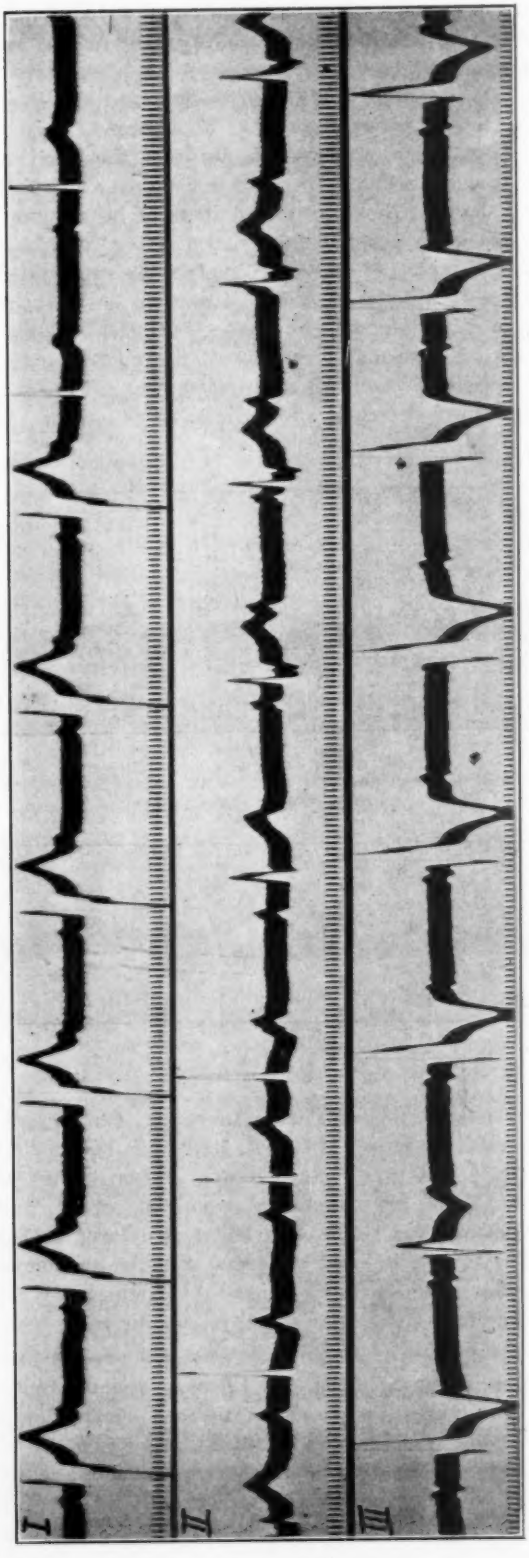

Fig. 2.—Leads I, II, III. Dec. 14. Periods of complete heart-block are shown in all three leads.

fell was shorter than that in which no ventricular beat was present. All the short P-R intervals were of equal duration as also were those of the longer interauricular periods. The intervals between the ventricular complexes were equal except at one point in Lead III where the second last complex illustrated appeared prematurely. The R-R interval between this complex and that which followed was equal to that between the other ventricular complexes. At some other points there was an apparent difference in the R-R interval but careful measurement showed that this was not so. The explanation was that the plate fell at a slightly uneven rate. The complex following the premature beat in Lead III had

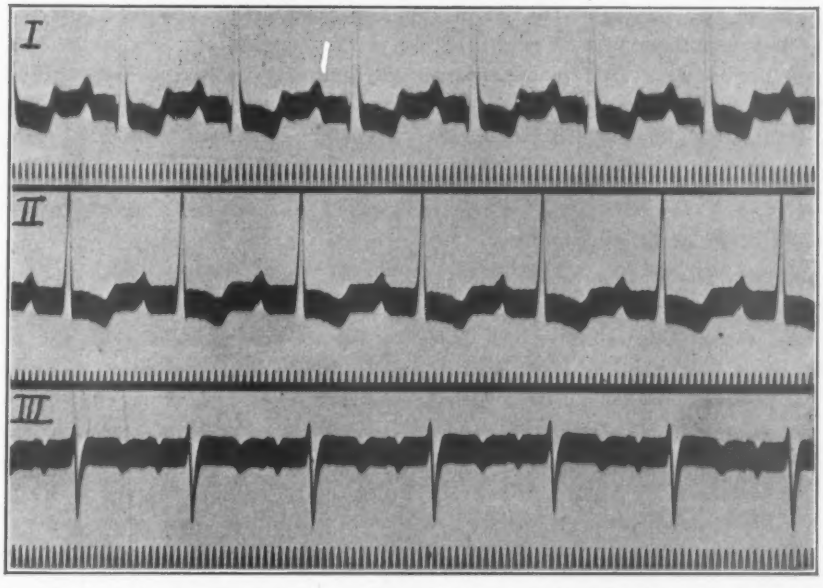

Fig. 3-*A*.—Leads I, II, III. Dec. 14. After atropine sulphate, 1/50 gr., hypodermically.

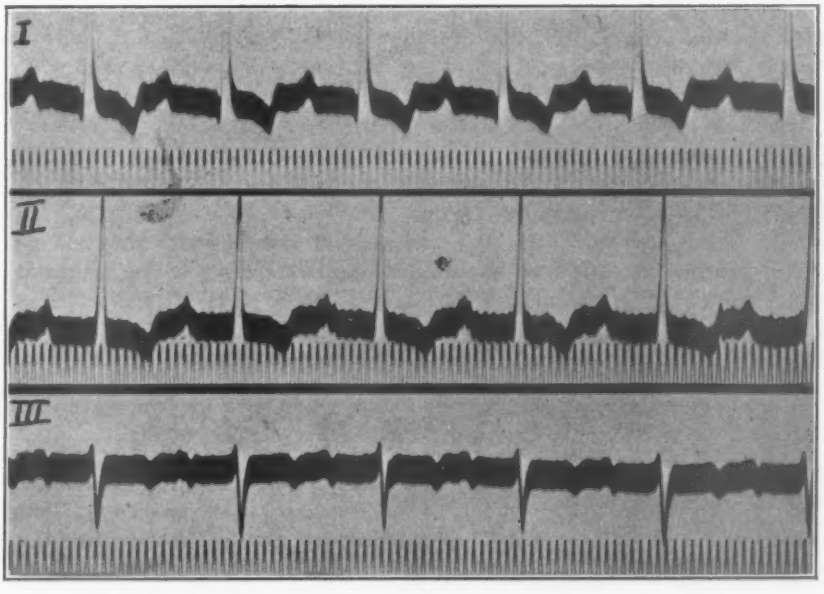

Fig. 3-*B*.—Leads I, II, III. Dec. 16. Exercise was given before each record was taken.

a slightly different form from the other abnormal complexes seen in this lead. The first complex in the period of dissociation in Lead II differed from the others in that R was rather broader and S was practically absent. The last complex was also slightly different, but this might be due to the fact that P was buried in it.

Vagal pressure in the neck was applied and complete dissociation continued as long as the pressure was maintained.

Atrophine sulphate, 1/50 gr., was given hypodermically at 4:10 P.M., and records were taken in rapid succession at first, and then every five minutes for an hour. Three minutes after the injection the ventricular rate had increased to 107 and the rhythm was regular. The heart rate remained about this level for the rest of the day and there was no return of the marked degree of block which had been present previously. During the normal rhythm after atropine well-marked left ventricular preponderance was seen and the P-R interval was reduced to 0.21 of a second. P was negative in Lead III and T was negative in all three leads (Fig. 3-*A*).

Dec. 15.—Every third to fifth auricular beat was blocked, but no periods of complete dissociation were observed.

Dec. 16.—The degree of block was the same as on the previous day. When atropine was given the increase in rate and reversion to normal rhythm were observed three minutes after the injection so it was thought that the change might be due to a psychic stimulus from the prick of the needle. As a control the patient was pricked with a needle several times without giving any drug, but no change in rate or rhythm was observed. Patient was exercised and the block was relieved temporarily. This was so transient, however, that it was only possible to take a record from one lead before the block had returned to its former state. Electrocardiograms were made in which exercise was given before each lead was taken. These were similar in every respect to those seen after atropine (Fig. 3-*B*).

Dec. 17.—The same degree of block persisted. The auricular rate was 110 and the ventricular 82. Adrenalin m. v was administered hypodermically at 3:38 P.M. At 3:41 the rate was 112 and the rhythm was normal. At 3:42 the rate had increased to 125, but a dropped ventricular beat appeared at long intervals. One abnormal ventricular complex was seen which seemed to arise from a focus in the right ventricle. From 3:45 to 3:54 dropped beats appeared at intervals and gradually became more frequent. Abnormal ventricular complexes were also seen. These had the same form as the ventricular complexes which had been observed previously during idioventricular rhythm (Fig. 4-*A*, *B*, and *C*). No abnormal ventricular beats were seen after this and at 4:04 the auricular rate had returned to its rate before the injection but dropped beats were much less frequent. The observation was terminated at 4:26.

Dec. 18-20.—Throughout this period every third to fifth auricular beat was blocked.

Dec. 20.—In the evening the patient had a slight rise of temperature and the ventricular rate increased to 120 while the rhythm became regular.

Dec. 21-22.—The same grade of block was present as formerly.

Dec. 23.—Patient developed the attack of headache accompanied by drowsiness described under clinical notes. Accompanying the rise of temperature the block completely disappeared.

Dec. 28.—The temperature was normal and the heart rate slower, but all signs of heart-block were absent. They remained so until digitalis was recommenced.

Jan. 7.—An electrocardiogram showed left ventricular preponderance, a P-R interval of 0.17 of a second, and a negative P in Lead III. T was positive in Lead I, iso-electric in Lead II, and markedly negative in Lead III.

Adrenalin, m. v, was given hypodermically at 3:56 P.M., and the heart rate increased from 126 to 148, but there was no change in the form of the complexes except that during the more rapid rate P and T were superimposed. No abnormal ventricular complexes were observed. The heart rate returned to its previous level at 4:24.

Jan. 12.—Patient was given atropine sulphate, 1/50 gr., hypodermically at 4:04 P.M. The rate before the injection was 126 and five minutes later fell to 110. It rose gradually to 147 at 4:35, after which it slowly declined. The complexes retained the same form throughout.

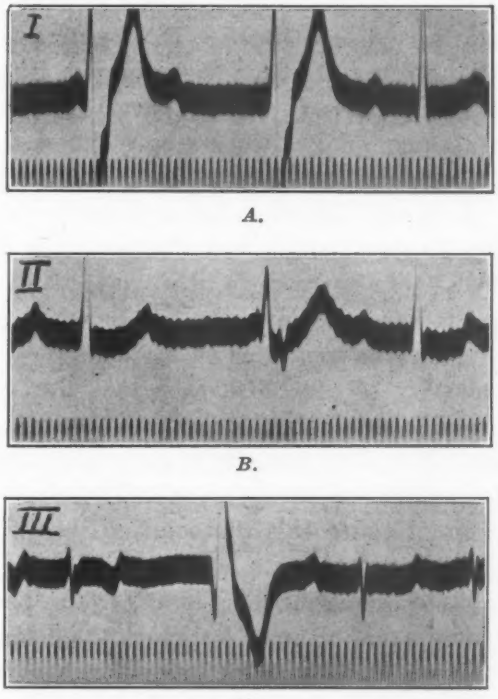

Fig. 4-*A*.—Lead I. Dec. 17. Ventricular extrasystoles following adrenalin administration. *B*, Lead II. Ventricular extrasystole following adrenalin administration. *C*, Lead III. Ventricular extrasystole following adrenalin administration.

Jan. 17.—Digitalis was recommenced. One drachm of the tincture was given and one drachm the following day. Thereafter m. xv was given t. i. d.

Jan. 20.—The P-R interval was 0.17 of a second, but T in Lead II was definitely negative.

Jan. 24.—The P-R interval had increased to 0.21 of a second, and T in Lead II was more markedly inverted.

Feb. 4.—Occasionally dropped beats had been present during expiration for five days, but their frequency was not increasing. The slightest excitement caused them to disappear and no tracings were obtained which showed them, although repeated attempts had been made. Patient had now received fifteen drachms of the same tincture of digitalis as formerly in nineteen days. Digitalis was discontinued for three days and then m. xv was given daily.

Feb. 14.—The P-R interval was 0.17 of a second, and the form of the complexes was the same as when patient was not under the influence of digitalis except that T in Lead II was slightly negative.

DISCUSSION

The principal features of interest in this case are the marked degree of heart-block, which was relieved by atropine, its prolonged duration, and the production of abnormal ventricular contractions by the administration of adrenalin.

Some degree of heart-block frequently takes place in patients under treatment with digitalis, particularly if, at the same time, there is damage to the conducting mechanism, but it usually rapidly disappears when digitalis is discontinued. In the present case, however, instead of decreasing after digitalis was stopped, the heart-block continued to increase. On the day digitalis was discontinued occasional abnormal ventricular complexes were seen. These always followed a dropped beat and appeared to have been due to the fact that a center in the ventricle had stimulated it to contract before the auricular impulse, following the one which was blocked, had arrived to stimulate the ventricle. These beats were of infrequent occurrence because as a rule the conducting mechanism had sufficiently recovered after a dropped beat to allow the ventricle to respond to a supraventricular stimulus. The severity of the block increased during the next three days and abnormal ventricular complexes became more frequent, while the following day short periods of complete dissociation between the auricle and ventricle were observed. The character of the ventricular contractions during this dissociation was similar to the isolated abnormal ventricular beats which had been seen previously. Periods of complete dissociation persisted for the next four days but were not seen thereafter, although a marked degree of heart-block still persisted. Every third to fifth auricular beat was blocked and this condition remained unchanged for the next nine days. Following the rise of temperature on Dec. 23 and subsequent days, the block completely disappeared. An advanced grade of heart-block was thus present for fourteen days after digitalis was stopped. Robinson[13] states that, as a rule, digitalis action persists for from two to twelve days after the drug is discontinued, but may continue for three weeks or more. In most cases, however, the evidence of continued digitalis action in the later stages is a prolongation of the P-R interval and changes in the T-wave. The long continued high grade of block shown by this case is very unusual.

The fact that vagal paralysis practically relieved the block even when complete dissociation was present shows that it was due chiefly to inhibition. The block was, however, not completely removed by atropine as the P-R interval was still prolonged to a slight extent.

It is uncertain whether the conduction time would have been still further reduced had the dose of atropine been greater. Marked general atropine effects were produced so it was considered inadvisable to increase the dose. It seems probable that a small part of the impairment of conduction was not due to inhibition. Two possible explanations of this defect are possible. One that there was a temporary lesion of the bundle of His of rheumatic origin, and the other that it was due to direct action of digitalis on the conducting mechanism. The former seems the more probable, as it was impossible, when a second course of digitalis was given after the acute stage of the rheumatic infection had passed off, to produce such a marked degree of block as had been present during the first course, although more digitalis was given. This explanation is also supported by the fact that in the first course the block appeared when patient had in the system considerably less digitalis than the quantity calculated to produce full therapeutic digitalization. The presence of an occasional dropped beat in the later stages of the second course and its disappearance on the slightest excitement point to the fact that the action was again of an inhibitory nature. This patient seemed to have a particularly sensitive cardioinhibitory mechanism and by its action on this digitalis was able to produce a profound alteration in the rhythm of the heart. Although the vagal action on the heart was so marked, it is interesting that other toxic signs of digitalis action, such as nausea and vomiting, were absent.

As a rule in complete heart-block the site from which the ventricle receives its stimulus is the bundle of His immediately below the block. The ventricular complexes thus present a normal form. In the present case the ventricular complexes were abnormal and the question arises whether the impulse arose in the common bundle and the dextrocardiogram was due to the left branch of the bundle being blocked or whether the site of impulse formation was in the right ventricle. The latter seems the more likely as isolated beats of the same nature were observed before complete heart-block was present. Owing to its early division into smaller branches block of the left branch is rare, and it is unlikely, although not impossible, that this branch would show signs of block at long intervals while the right branch remained unaffected. Also similar ventricular contractions were elicited by a small dose of adrenalin, and Kahn[8] has shown that extrasystoles could be produced in the dog's ventricle by adrenalin. The doses which he used were very large, but Steward and Rogoff[14] found that the ventricle was more sensitive to adrenalin after digitalis had been given. In one experiment, in which extrasystoles appeared after digitalis administration, these could be removed by excluding the blood from the suprarenal glands from the general circulation and reappeared when adrenalin was admitted again to the circulation.

In the advanced stages of digitalis poisoning it is known that ventricular extrasystoles appear and that ventricular tachycardia may supervene. This is due to a direct action of digitalis on the heart muscle which may cause a focus in the ventricle to give out impulses at greater rate than the normal pacemaker, so that the former controls the ventricular rate. In the present instance the idioventricular rate was about 50, so that if defective conduction had been absent the ventricle would have responded normally. It is possible that the reason why the stimulus arose in the right ventricle is that direct action of digitalis on the heart caused a focus in this ventricle to send out impulses more rapidly than those emitted from the bundle below the site of the block. This is suggested by the fact that the rate of the ventricle in this case was higher than usually takes place during complete heart-block. It is interesting in this connection to consider whether, instead of the ventricle responding to a new rhythm center during the period of complete dissociation, the ventricular contractions were due to a circus movement as has been suggetsed by Lewis.[9] According to the latter view the idioventricular rhythm would be explained by the fact that one ventricular beat had escaped owing to defective conduction, and that this beat had caused the subsequent abnormal ventricular contractions. Auricular impulses during this time failed to affect the ventricle until one arrived at a time when the ventricle was in such a state that it could respond to it. The ventricle then continued to respond to supraventricular stimuli for a period of variable duration. If the beats were of a reentrant nature each wave circulated in the same path at the same rate except during part of the period of complete block shown in Fig. 2, Lead III. In this a premature beat took place and this was followed, after an interval similar to that between the other beats of the series, by a complex which differed slightly from the others. If circus movement were taking place the wave must have circulated more rapidly along the usual path in order to cause the premature beat, as the complex which preceded it was the same as the others while the changed form of the complex following the premature beat was due to the wave taking a slightly different path.

SUMMARY

A case of acute rheumatic fever is described which showed an advanced degree of heart-block while under treatment with digitalis. After the administration of digitalis was stopped the block increased for a few days until periods of complete dissociation were present. This condition lasted for four days and a severe grade of block continued for fourteen days after the discontinuance of digitalis. The block was due principally to inhibition, but it is suggested that a slight lesion of the bundle of His was also present which disappeared

later. A small dose of adrenalin produced ventricular extrasystoles during the time the patient was under the influence of digitalis and heart-block was present, but failed to do so at a later date when no block was evident and patient was free from digitalis.

I wish to thank Prof. G. Lovell Gulland for permitting me to make these observations, and the trustees of the Clinical Medicine Research Laboratory for permission to work there. The expenses of the work were defrayed by a grant from the Earl of Moray Research Fund, Edinburgh University.

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DESTRUCTION OF THE SINOAURICULAR NODE IN DOGS' HEARTS BY RADON*†

An Histological and Electrocardiographic Study

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OUR object was to determine the amount of sinoauricular node essential to its pace-making function, destruction being produced with radon.

For a summary and bibliography of the subject of sinoauricular destruction, reference may be had to Sir Thomas Lewis' monograph,[1] and to a review by Eyster and Meek.[2] In a recent paper,[3] one of us has expressed dissatisfaction with the method of ligation and surgical excision in partial destruction of the node. For a more thorough statement of the histological changes produced by radon in the sinoauricular node and surrounding tissues, the reader is referred to another publication.[4]

METHOD

Under aseptic conditions, using intermittent air-ether intratracheal insufflation supplied by an Erlanger respiratory tank, three or four centimeters were excised laterally from the costochondral junction of the right third or fourth rib, in a series of fourteen dogs. The visceral pleura was incised and the pericardium exposed. Injury to the right phrenic nerve was avoided in opening the pericardial sac, the edges of which were temporarily sewed to the wound margins. Occasionally, it was necessary to pass a silk suture through the fat in the A-V groove, well down on the right lateral aspect, and out through the anterior chest wall close to the sternum. When taut, this suture rotated the heart, exposing the site of the sinoauricular node. A small pocket was prepared by inserting the point of a needle just beneath the epicardium overlying the node. The needle was withdrawn, and a radon implant tube contained within a larger glass capillary tube 1 centimeter in length, to facilitate handling, was inserted with ordinary tissue forceps into the partially prepared pocket. The tube was anchored by forcing it further on into the intact tissue. In the two control experiments, capillary tubes without radon were used. The radon tubes varied in strength from 0.6 to 5.0 millicuries, and were left in place permanently. The pericardium, pleura, muscle, and skin layers were closed separately.

Electrocardiograms were taken before and after operation. In a few instances where it was believed that the node had been destroyed, the effect of cooling the head, body, and tail of the node with a U-shaped glass tube containing circulating ice water was noted.

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†Preliminary report read by Dr. E. B. Krumbhaar before the Federation of American Societies for Experimental Biology, at Cleveland, Ohio, December 30, 1925.

After postmortem examination, the region of the sinoauricular node and surrounding tissue were fixed in formalin (5 per cent) and mounted in paraffin. Serial sections of ten micra thickness were cut at right angles to the linea terminalis through the crista terminalis and stained semiserially with hematoxylin and eosin, and van Gieson-hematoxylin stains.

DATA

The following protocol on Dog 10 illustrates the method used:

Dog 10 was operated upon Feb. 4, 1925, one day following a normal electrocardiographic study. A tube containing 2.0 mc. of radon was introduced subepicardially over the sinoauricular node. On July 21, 1925, resection of the right vagus nerve was done. Oct. 10, 1925, tracheotomy and thoracotomy were performed. Adherent pleura and pericardium were dissected from the node, following which the tail, body, and head of the node were cooled. Death followed drowning with ether intratracheally. The area about the node was placed in 5 per cent formalin, and forty-eight hours later was photographed (see Fig. 1). The radon tube was never recovered, and there was no evidence of its presence in the x-ray plates of the

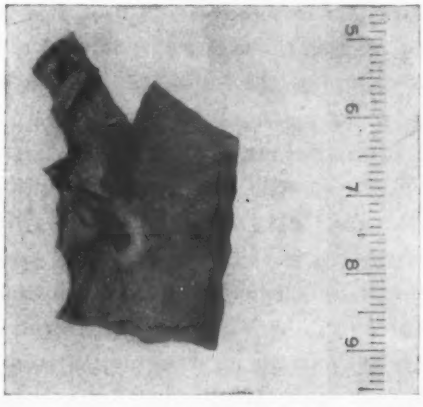

Fig. 1.—The sinoauricular junction in Dog 10 forty-eight hours after 5 per cent formalin fixation. The crescent-shaped scar, which replaced the underlying crista terminalis containing the sinoauricular node, was produced by a 2.0 mc. radon tube which was allowed to remain in place until postmortem 240 days after time of introduction.

tissue. A paraffin block of the tissue was made, and serial sections were cut and stained. The crescent-shaped scar visible grossly was seen microscopically to be made up of connective tissue, considerably hyalinized, surrounded by fatty change and hemorrhage.

Table I summarizes the electrocardiographic studies on Dog 10.

The combined histological and electrocardiographic data on all the animals are summarized in Table II.

DISCUSSION

The foregoing data may be considered as follows:

A. *Experiments Where There Were No Postoperative Electrocardiograms.*—Through error the radon tube was left in place twenty-two days after death in Dog 4 while the node was in formalin, with only eight hours exposure to radon in vivo. The histological changes ob-

TABLE I

(DOG 10)

DATE	CONDITION	P-R INTERVAL	RATE	REMARKS
2- 3-25	Normal pre-operative	0.09-0.10	80-100	Marked sinus arrhythmia.
2- 5-25	Normal post-operative	0.10-0.11	130	Slight sinus arrhythmia.
2-13-25	Normal	0.00-0.08	60-80	Marked sinus arrhythmia. Occasional cycles of zero P-R intervals and slowed cardiac rate.
6-17-25	Normal	0.09	110	Marked sinus arrhythmia. Inverted T-waves.
8-21-25	Under ether	0.09	165	One cycle of S-A block.
8-21-25	One month after right vagus cut	0.08	120	Sinus arrhythmia.
10-10-25	Under ether	0.10	200	
10-10-25	Cooling S-A node	0.00	Much slowed	Interpreted as ventricular escape or cycles of nodal rhythm.

served in this animal were similar in every respect to those in other animals except for the lack of hemorrhage and scar tissue. This suggests that the action of the radium emanation may be primary upon the cell as well as secondary through the circulatory changes it produces.

Nodal tissue 5.95 mm. in length was observed in Dog 6, together with engorgement of the small vessels and hemorrhage. In the tail of the node, vacuolization, fatty change, cell shrinkage, necrosis, and scar formation were observed. These changes occurred after the introduction and retention of the empty glass control tube.

In Dog 8 no nodal tissue was seen. Neither was the tube found. There were hemorrhage, necrosis, fragmentation, pigmentation and round-cell infiltration which might be considered incident to the introduction with retention of the tube. Eight millimeters of node were seen in Dog 14, with hemorrhage, fatty change, necrosis, and sclerosis of the caudal part of the node. The more extensive change might be attributed to the 5.0 mc. strength of radon.

B. *Experiments Where There Were Postoperative Electrocardiograms.*—The P-R interval which one of us has determined in a series of seventy normal dogs has varied from 0.07 to 0.13 of a second. The P-R interval in the individual normal animal has varied as much as 0.03 of a second in a single tracing. Cardiac rates in normal dogs vary from 80 to 130 per minute. Interpretation of any findings must take these variations into account.

If we accept the work of Eyster and Meek,[5, 6] the reduction of the P-R interval in an individual dog from 0.09-0.11 of a second to 0.07-0.09 of a second, accompanied by a fall in cardiac rate, suggests that the seat of the impulse is probably in the coronary sinus region of the atrioventricular node. Such an interpretation might be applied to the following animals in these experiments:

Dog 2 (P-R interval decreased from 0.09-0.12 sec. to 0.08-0.09 sec. cardiac rate decreased from 100 to 60 per minute).

Dog 7 (P-R interval decreased from 0.12-0.13 sec. to 0.08-0.10 sec. cardiac rate unchanged at 120).

Dog 10 (P-R interval decreased from 0.09-0.10 sec. to 0.00-0.08 sec. cardiac rate decreased from 100 to 70).

This interpretation is further substantiated by the absence of any nodal tissue and its replacement by scar tissue observed in each of these animals, and because in the normal dog a reduced cardiac rate is associated with an increase in the P-R interval rather than a decrease as noted in the above three dogs.

The work of Flack,[7] Ganter and Zahn[8] and Zahn[9] showed among other things that cooling the region of the sinoauricular node in normal mammalian hearts produced a reduction or disappearance of the As-Vs interval. Zahn further determined that the seat of impulse initiation had moved from the sinoauricular region to the mouth of the coronary sinus in which place Koch observed nodal tissue.

It would therefore be expected that in cooling the node in Dog 10 in our series no effect would be produced, inasmuch as it was believed that the impulse was initiated at the coronary sinus rather than at the sinoauricular node. Cooling the sinoauricular node in this dog, however, produced zero P-R interval and slowed the cardiac rate. (Fig. 2.) The rhythm subsequent to cooling might be interpreted as atrioventricular or complete sinoauricular block with ventricular escape. Neither interpretation, however, alters the fact that the rhythm prior to cooling was initiated by the sinoauricular region, which subsequently *failed to show the slightest remnant of nodal tissue upon histological examination.*

In Dog 11 no especial change in P-R interval or cardiac rate occurred postoperatively. Cooling the head of the node produced no change, but cooling the body or tail produced a zero or negative P-R interval, and slowed the cardiac rate. Stretching the tissues by exerting pressure downward upon the region of the sinoauricular node with the cooling tube at normal temperature produced no change in the P-R interval or cardiac rate. When ice water was allowed to flow through the tube, the changes noted above were produced. These changes occurred more quickly when the region of the tail of the node was cooled than when the region of the body was cooled, sugesting that the area of impulse initiation was in the former. (Fig. 3.) Histologically, no nodal tissue was observed in this animal.

From the foregoing findings it would seem that complete destruction of the sinoauricular node as revealed by histological examination may not always be deducted from the electrocardiogram. It is remotely possible, however, that a sinus rhythm may be initiated by

TABLE II

NO.	STRENGTH OF RADON IN MILLI-CURIES	NO. DAYS LIVED	CAUSE OF DEATH	ELECTROCARDIOGRAMS				REMARKS	HISTOLOGICAL CHANGES
				PREOPERATIVE		POSTOPERATIVE			
				P-R INTERVAL IN SECONDS	HEART RATE PER MINUTE	P-R INTERVAL IN SECONDS	HEART RATE PER MINUTE		
1	2.0	10	Fibrinous pericarditis and pleursy	0.10-0.11	100	0.08-0.11	160	No changes in rhythm; died on tenth day	Vascular engorgement with free hemorrhage into head of node. Fatty change, hemorrhage, endothelial infiltration, necrosis, new connective tissue, in body and tail of node
2	2.0	180	Etherized	0.09-0.12	100	0.08-0.09	60	Marked sinus arrhythmia during first week postoperative. Occasional cycles of nodal rhythm or ventricular escape during the fifth month	No nodal tissue identified; entire crista terminalis replaced by hemorrhage, fatty change, necrosis, advanced fibrosis with hyalinization and calcification and occlusion of nutrient vessel
3	1.38	3	Empyema	0.10-0.11	120	0.07-0.10	120	Died too early	Nodal tissue 1.8 cm. in length observed. Fatty change with endothelial cellular infiltration into the body of the node
4	0.60	8 hr.	Pneumonia	0.07-0.09	120			Died too early	(Tube left in place 22 days during formalin fixation.) No node seen; replaced by areas of necrosis
5	1.3	49	Chloroform	0.09-0.10	130	0.08-0.12	140	No abnormalities in rhythm	No marked pathological changes. Believe tube not retained
6	Blank	3	Pneumonia and Empyema	0.09-0.10	100			Died too early	5.75 mm. of upper part of node seen. Observed moderate engorgement with hemorrhage, vacuolization, shrinkage of cells and nuclei, necrosis and new scar tissue

TABLE II—CONT'D

NO.	STRENGTH OF RADON IN MILLI-CURIES	NO. DAYS LIVED	CAUSE OF DEATH	ELECTROCARDIOGRAMS				REMARKS	HISTOLOGICAL CHANGES
				PREOPERATIVE		POSTOPERATIVE			
				P-R INTERVAL IN SECONDS	HEART RATE PER MINUTE	P-R INTERVAL IN SECONDS	HEART RATE PER MINUTE		
7	0.98	90	Chloroformed	0.12-0.13	120	0.08-0.10	120	Varying shaped P-waves postoperatively	Node replaced by fatty change, necrosis, connective tissue
8	1.45	5	Empyema	0.07-0.08	100			Died too early	Node replaced by hemorrhage and necrosis. Some pigmentation and round-celled infiltration
9	1.0	36	Stitch abscess Acute glomerular nephritis	0.08-0.09	110	0.10-0.11	150	Inverted T-waves	Entire crista replaced by hemorrhage, fatty change, necrosis, fibrosis, hyalinization, calcification, and thrombosis
10	2.0	240	Etherized	0.09-0.10	100	0.06-0.09	70	On ninth day ventricular escape or nodal rhythm	Fatty change, necrosis, hemorrhage, cicatrization, hyalinization, vascular occlusion
11	3.4	210	Etherized	0.09-0.12	100	0.10-0.11	100	Postoperatively flat P-waves	Hemorrhage, fatty change, necrosis, scarring, and hyalinization
12	1.85	210	Etherized	0.10-0.12	100	0.10-0.11	120	No abnormalities noted	Nodal tissue 9.35 mm. seen. No marked changes. Tube perhaps not retained
13	Blank	210	Etherized	0.08-0.11	90	0.09-0.10	120	Preoperative inversion of T-waves seen	Normal node 5.25 mm. seen
14	5.0	7	Pneumonia	0.09-0.11	110			Died too early	8.0 mm. node seen with caudal replacement by hemorrhage, fatty change, necrosis, and scar tissue

nodal tissue too minute for histological detection. It is further possible under the conditions of these experiments that the tissue immediately about the sinoauricular node may have originated the cardiac

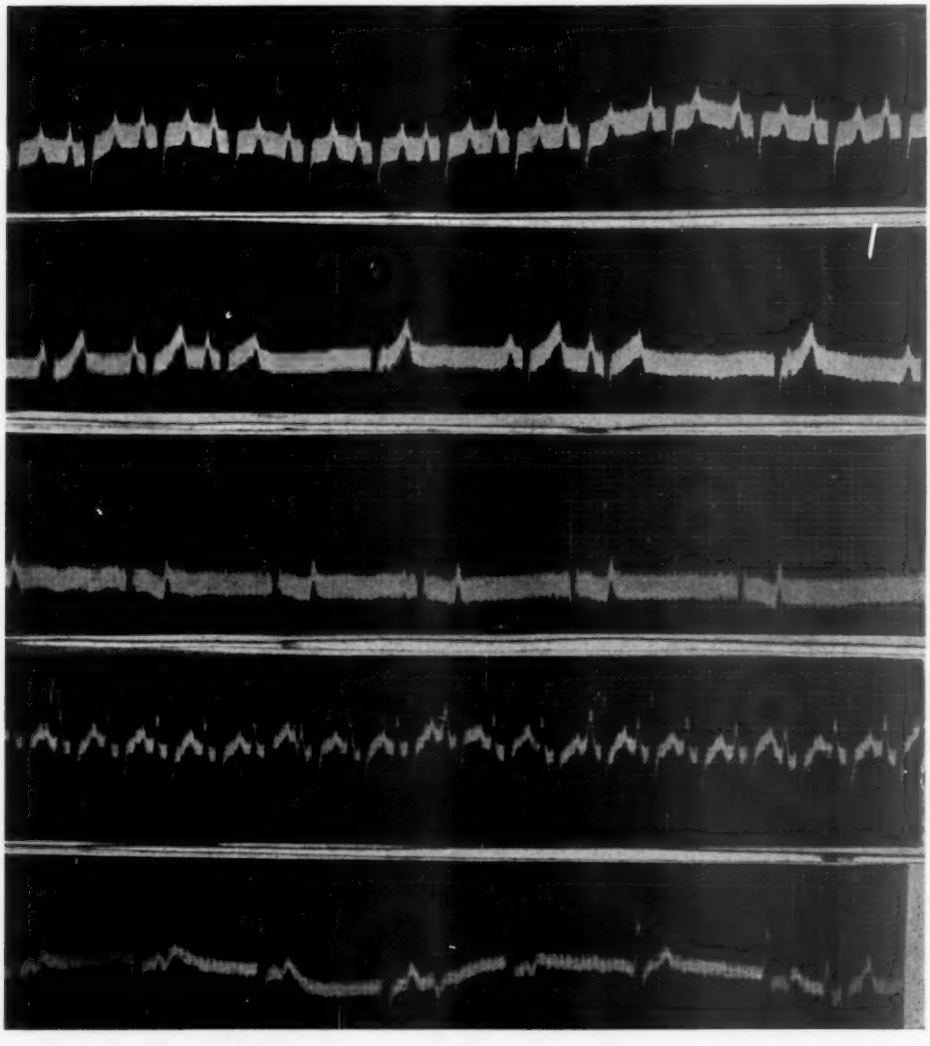

Fig. 2.—Electrocardiograms on Dog 10.

Strip 1: Preoperative tracing on normal dog, showing normal electrocardiogram.

Strip 2: Postoperative tracing nine days after introduction of a 2 mc. radon tube over sinoauricular node. Cycles 4 and 7 are abnormal. An abnormally shaped P-wave is seen after the QRS complex. These two cycles may be considered nodal in origin, or they may be due to sinoauricular block with resulting ventricular escape. This latter opinion is substantiated by the prolonged time intervals between the third and fourth cycles and the sixth and seventh cycles.

Strip 3: Tracing was taken the same day Strip 2 was obtained, 69 minutes after ½ gr. morphine sulphate, and 6 minutes after 1/50 gr. atropine sulphate were given intramuscularly, the effect of the latter drug being superimposed upon the former. A varying P-R interval, and a variably shaped P-wave are seen. Apparently the dominant rhythm was sinus in origin.

Strip 4: Tracing, obtained 240 days after operation, shows a normal sinus rhythm.

Strip 5: Tracing, obtained shortly after Strip 4, shows nodal rhythm; the result of cooling the sinoauricular node, is further evidence of the sinus origin of the rhythm. Histologically, there was no sinoauricular nodal tissue present in this animal, the crista terminalis being replaced by a hyalinized scar.

impulse. It should be noted that the pathological changes observed were so extensive in all blocks of tissue that only a narrow fringe of relatively normal auricular and vena caval tissue was seen at a distance of from seven to eight millimeters lateral to the linea terminalis.

Possible errors in technic may be considered. Some nodal tissue might have been present but unobserved. In answer, we can only state that we have never had any difficulty in finding nodal tissue in the normal animal or in others where pathological changes existed in

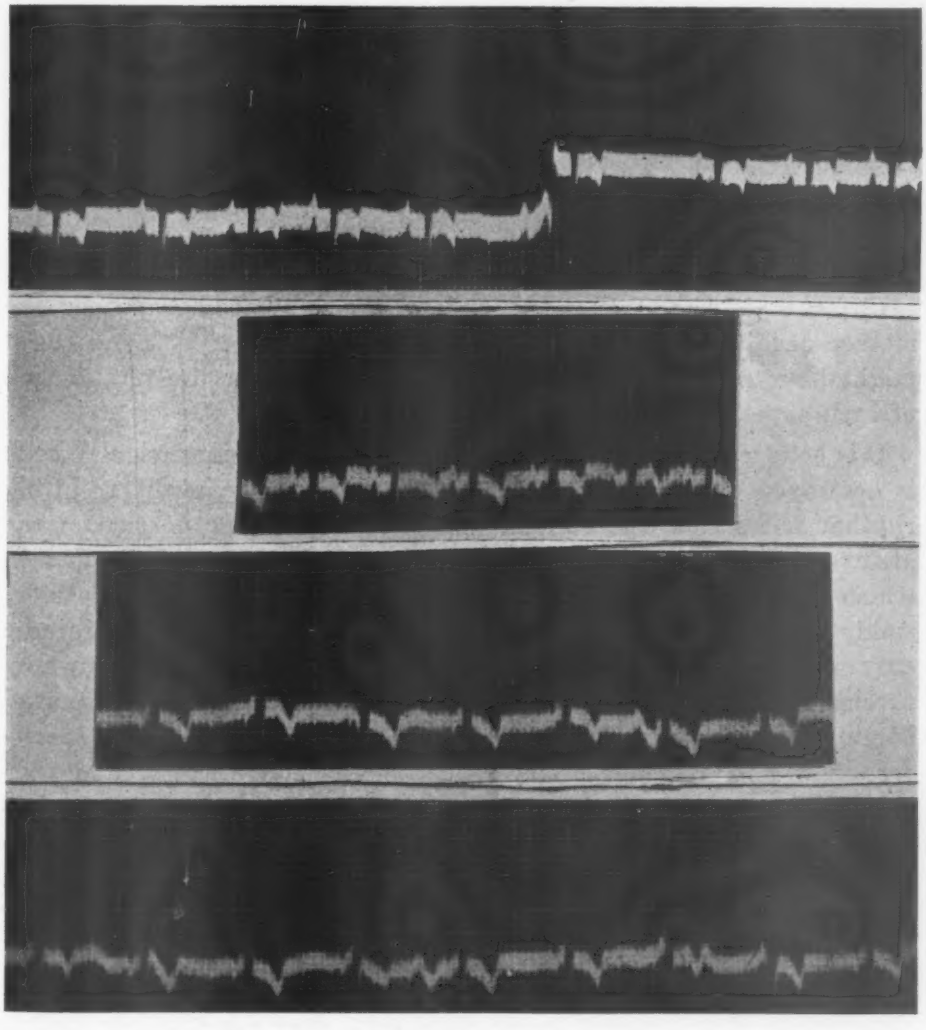

Fig. 3.—Electrocardiograms on Dog. 11.

Strip 1: Normal preoperative electrocardiogram.

Strip 2: Normal electrocardiograms obtained 210 days postoperatively under ether anesthesia.

Strip 3: Taken immediately after Strip 2, showing the effect of cooling the body of the sinoauricular node. There is an inverted P, and the P-wave is occasionally difficult to distinguish if present.

Strip 4: Taken immediately after Strip 3, showing effect of cooling the tail of the sinoauricular node. P is inverted or absent.

Histologically, this dog showed no sinoauricular nodal tissue.

or about the sinoauricular node. It might be thought that deformity incident to scar formation rendered orientation difficult, but marked twisting or alteration in the course of the muscle fibers incident to scar formation was never observed. The anatomical proximity of the coronary sinus region to the sinoauricular node may leave the method employed in cooling the node open to possible criticism. The cooling, however, was carried out very carefully, the cooling point being a glass bulb 7.0 mm. in diameter on the base of a hollow U-shaped glass tube through which ice water circulated. This cooling point could be accurately placed, and the only possible way for the cooling effect to reach the coronary sinus was by contiguity of tissue, a distance of at least five centimeters. This is a very remote possibility. The production of nodal rhythm by these cooling experiments in dogs which prior to cooling gave electrocardiographic evidence of sinus rhythm and at postmortem examination showed complete ablation of the sinoauricular node suggests that the conclusions drawn from all previous cooling experiments may be erroneous.

Unfortunately, we possessed only one electrocardiograph, or the method of initial negativity employed by Lewis[1] and Eyster and Meek[6] might have given further functional information at the termination of each experiment.

It is believed that when the normally functioning sinoauricular node is destroyed or functionally depressed, the impulse in the resulting rhythm arises from the coronary sinus or ventricular portion of the atrioventricular node. This opinion is based upon experiments in which the destruction or functional depression has been relatively sudden as observed in excessive vagal stimulation by drugs or faradic current, or destruction, partial, or complete, of the nodal structure by thermal, chemical or mechanical means. In the experiments reported herein, *rhythmic changes were brought about slowly by an agent heretofore unused for that purpose whose destructive action was gradual during the course of about thirty days.* The functional result might reasonably be expected to be different. Gradual destruction is a process much less open to the criticism heretofore directed against sudden experimental destruction of the nodal tissues voiced more especially by Sir Thomas Lewis.[1]

It is entirely possible that these long time experiments with slow destruction of the sinoauricular node may alter some of our beliefs concerning the production of the normal cardiac impulse. Apparently normal electrocardiograms from a dog showing complete destruction, histologically, of the sinoauricular node, have never been noted in the past. It is an impossible finding from the point of view of our present interpretation of the production of the cardiac impulse. We are fully conscious of the scrutiny and criticism our data may

receive. It is possible, however, that the slow destructive process used in these experiments offers an explanation for the phenomenon, and if that is true it will, no doubt, be the explanation for the changes occurring clinically in most disease processes, apart from embolism or sudden thrombosis of the nutrient vessels of the sinoauricular node.

Our data are incomplete for the early effects of radon upon the sinoauricular node as seen in the electrocardiogram. It is possible that there may be early stimulation or depression either of the nodal cells, the vagal fibers ending in the node, or some vascular change which might be revealed by frequent electrocardiograms immediately after the radon application. Changes in rhythm may also occur so gradually as not to be present until the end of the second or third week after operation, and because they are so gradual they may not be detected in the electrocardiogram. Further, the value of determining the site of impulse initiation by the initial negativity method whether or not the animals show electrocardiographic evidence of disturbances of rhythm is obvious. One of us (Borman) and Walter J. Meek are at present attempting a solution to some of the questions raised by these experiments, and the results of our study will be the subject of a further report.

CONCLUSIONS AND DEDUCTIONS

1. A method of experimental destruction of the sinoauricular node through the gradual and limited action of radium emanation is herein presented.

2. Complete destruction of the sinoauricular node as evidenced by present histological methods may not always be detected in the electrocardiogram.

3. Complete histological destruction of the sinoauricular node under the conditions of the foregoing experiments may be ultimately followed by a rhythm functionally simulating a typical sinus rhythm.

4. When part of the sinoauricular node has been destroyed by radon, the finding of a normal electrocardiogram suggests that the cardiac impulse may be initiated by sinus tissue too minute to be detected histologically.

5. When the sinoauricular node has been gradually destroyed by radon, the possibility of the intact surrounding cardiac tissue initiating the impulse must be considered.

6. Exposure of the sinoauricular node in the dog to radon may produce changes in cardiac rhythm represented in the electrocardiogram by cycles of sinoauricular block, nodal rhythm, and possible coronary sinus rhythm.

7. In apparently normal dogs the P-R interval may vary from 0.07 to 0.13 of a second; in a single electrocardiogram, there may be a

normal variance in the P-R interval of 0.03 of a second; the cardiac rate may vary from 80 to 130 beats per minute in the normal dog.

We wish to thank Dr. J. E. Sweet and Dr. E. B. Krumbhaar for their interest and suggestions offered during the course of these experiments. We are particularly indebted to Dr. Sweet, who first suggested the use of radon for the purpose of these experiments, and to Miss Margaret Clemens, electrocardiographic technician, whose patience made many of our records possible.

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METASTASES TO THE HEART FROM MALIGNANT TUMORS*

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SECONDARY involvement of the heart due to neoplastic change is not a common occurrence. The condition is occasionally seen in widespread involvement of other organs; it is, however, seldom suspected by any symptoms, directly or indirectly related to the cardiovascular system. Metastases to the heart are more common than primary neoplasms of that organ, and of the secondary tumors, carcinomas are more common than sarcomas. Necropsy records of large groups have established fairly definitely the relative incidence.

The statistics here quoted are taken from Peters and Milnè[1] as many of the original references are unavailable. Blumensohn in a review of 1,078 cases of carcinoma in general found secondary heart involvement in 34, while from 160 cases of sarcoma, 12 showed cardiac metastases. Chambers in 2,161 autopsies found secondary carcinoma of the heart in 7 cases. Willigk in 4,547 autopsies, 6 cases; Pic and Bret in 1,708 autopsies, 25 cases; Thorel in 3,000 autopsies, 15 cases; Tadson in 8,289 autopsies, 6 cases; and in the last 1,976 autopsies in the Russell Sage Institute, New York, only 3 cases have been observed.

Bryant[2] states that Ely found among 2,161 autopsy records, 7 cases of cardiac tumor, all being secondary carcinomatous metastases (Georg. Hosp. records 10 yrs.) and among the 2,942 autopsies in the Johns Hopkins Hospital (1907) there were 10 tumors of the heart, all secondary with the exception of one rhabdomyoma. Karrenstein[3] in 6,655 autopsies performed at the Pathological Institute of the University of Berlin found 15 secondary carcinomas of the heart and 4 secondary sarcomas. In 3,000 autopsies at the Stanford Medical School there have been 5 tumors of the heart, all secondary. Of these tumors, 2 were carcinoma and 3 sarcoma.

The more recent articles on primary tumors of the heart present a systematic review of the subject. There is some difference of opinion as to whether many of the tumors reported by earlier writers were real blastomas or only organized thrombi which had undergone a certain metamorphosis. Suffice it to say that about 150 cases of primary tumor have been reported and among these, as gathered from a review of the literature by Link[4] (1908), Ehrenberg[5] (1911), Perlstein[6] (1918), Goldstein[7] (1922), Beck and Thatcher[8] (1925) there are about 40 cases of sarcoma. Fibromas, myxomas, and fibromyxomas are the most

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frequent; rhabdomyomas, lipomas, angiomas, and teratomas are rare. From a review of the above statistics, one is convinced of the relative infrequency of malignant tumors of the heart. We find that primary newgrowth is less frequent than metastatic neoplasms.

It is of interest to note that metastases to the heart have occurred from all the principal organs of the body in which malignant disease is commonly found. Linell[9] reports cardiac involvement from carcinoma of the trachea; Lisa,[10] from carcinoma of the tongue; Wagner,[11] from carcinoma of the submaxillary gland; Pic and Bret,[12] from rodent ulcer of the face; Moore,[13] Siegel-Delval and Marie,[14] carcinoma of the esophagus; Peters and Milne,[1] Moore,[13] Widal and Abrami,[16] carcinoma of the stomach; Barthelemy,[17] carcinoma of the pancreas; Peters and Milne,[1] carcinoma of the rectum; Hektoen,[18] Kapsinow,[19] Goldstein,[7] Ehrenberg,[5] carcinoma of the breast; Rist and Rolland,[20] carcinoma of the uterus; Caussode, Surmont and Lacapere,[21] Bosco,[22] carcinoma of the lung; Kanthach,[23] carcinoma of testes; Batzdorff,[24] hypernephroma; Moore,[13] Rabé and Morel,[25] sarcoma of the kidney; Allyn and Karsner,[26] sarcoma of skin; Delhern and Laignel-Lavastine,[27] sarcoma of skin; Aubertin,[28] Peters and Milne,[1] sarcoma of lymph glands; Hektoen,[18] Allyn and Karsner,[26] sarcoma of bone; LaPlace and Karsner,[29] Goldstein,[7] sarcoma of bone; Pomay-Michaux and Boué,[30] sarcoma of pleura; Goldstein,[7] sarcoma of eye; Warthin,[31] sarcoma of nasal passages; Tedeschi,[32] sarcoma of sternum; Goldstein,[7] pigmented soft mole of labium majus; Bardenheuer,[33] sarcoma of ilium.

Bodenheimer found the muscular walls of the heart most often affected and felt that the right heart was attacked as often as the left but Napp[34] thinks that secondary malignancy has a predilection for the right heart, especially the ventricle, in contrast to primary tumors which frequently involve the auricle.

Secondary tumors vary in size, shape, and appearance. They are frequently found as small, whitish, shotty accumulations of cell growth. They are widely scattered throughout the muscular walls, in close proximity to the vascular supply (Aschard and Mouzon[35]) (Warthin[31]). Large polypoid types occasionally encroach upon a chamber of the heart (Pommay-Michauz and Boué[30]) or become engrafted upon a valve, producing large vegetations like infectious endocarditis (Widal and Abrami[16]), (Rist and Rolland[20]), (Kanthack[23]). A pedunculated tumor or a metastatic deposit lying free in the heart cavity (Warthin[31]) may act as a ball-valve. A secondary growth may occasionally outstrip the primary growth.

The histological structure of the primary neoplasm, as a rule, is reproduced with considerable fidelity by the metastatic nodule. In rare cases the superficial lymph vessels of the heart and pericardium stand out like whitish threads due to cancerous lymphangitis (Auber-

tin[28]), or the pericardium may become thickened and leathery due to scirrhous involvement. The pericardial fluid may then be hemorrhagic (Kapsinow[19], Bosco[22]).

Cardiac metastases are considered to be blood-borne in the majority of instances. Lanceraux and others have found tumor cells in the circulating blood; von Recklinghausen has noted sarcoma tissue in the right ventricle growing upon the endocardium between the papillary muscles, and Tedischi found small bits of tumor in blood clots (Peters and Milne[1]). There is indisputable evidence that cancer cells have formed the center of a thrombus (Menetrier and Gauckler[36]). I noted, in a case of carcinoma of the stomach, that strands of tumor cells could be demonstrated in the lumen of the coronary vessels without any gross evidence of metastatic nodules in the proximity. There are, however, only a limited number of case reports of neoplastic thrombosis of the heart (Kanthack,[23] Warthin,[31] Aubertin[28]) which offer proof of this blood-borne invasion.

It is of interest to note that many cases here reviewed, as also the cases reported below, are associated with primary or secondary intrathoracic neoplasms; i.e., lung, pleura or mediastinal lymph glands. Pic and Bret[12] stressed this point in an earlier contribution. The relative frequency of lung metastases as compared with relative infrequency of secondary involvement of the heart allows one to surmise that the lungs and adjacent tissue support the growth of cancerous tissue more effectively than the tissues of the heart and therefore become involved at an earlier date in the progress of the disease. The heart is one of the organs which is especially unsuited to the growth of tumor cells although this organ must receive many tumor emboli. Possibly the vascularity of the heart is in some way related to this relative infrequency of metastases. (See Burrow's recent work.[37])

Assuming that the lungs, pleura, or mediastinal lymph glands are involved at an earlier date than the heart, the pulmonary veins probably act as a means for tumor cell conveyance; first to the left auricle, then to the left ventricle and finally via the coronary circulation to the heart muscle. Implantation grafts which are found in the endocardium of the right heart occur by a different mechanism. In these instances neoplastic emboli gain entrance to the blood stream through the lymphatic duct, the bronchial veins or the azygous veins and thence through the superior cava to the right auricle and ventricle (Hektoen[18]). Implantation of a graft upon the endocardium of the right heart and subsequent distribution of metastatic masses into the lungs from time to time is a rarer possibility, although the cases of Delherm and Laignel-Lavastine,[27] Rist and Rolland,[20] and Warthin[31] suggest such a mechanism.

A much smaller number of metastases to the heart occurs by lymphatic conduction. In this connection it is important to recognize that

the tracheobronchial glands drain the pleura, lungs, myocardium, and pericardium and that this system offers a means of secondary invasion to the heart by retrograde conduction from tumors of lungs and pleura. Cancerous lymphangitis in which the dilated tracts from the heart are filled with tumor cells as in the cases of Aubertin[28] and of Wolf and Giet[15] are examples of conduction by this mechanism.

Direct extension is the third means of cardiac invasion by malignant growth. How great a rôle the lymphatic system plays in direct extension of tumors from the mediastinum to the heart is not known. Actual extension of an invasive tumor occurs through the growth of strands of tumor cells into the interstices of the surrounding tissue. As a rule these strands of cells maintain their continuity. With the widening of the strands, the peripheral parts of the tumor become more condensed and the intervening normal tissue is destroyed. At times the advancing margin is more compact and the normal tissue is largely pushed aside and compressed, so that the tumor grows by the invasion of coarse, projecting masses. In many instances these masses, as well as the finer strands, are guided by meeting with a dense fascia or other resisting tissue, along the surface of which they spread.

This mechanism of invasion of the heart is possible with tumors which are primary in the lungs or mediastinum or which have secondarily involved the lymph nodes of that region. In general, however, the heart is seldom involved by continuity and contiguity from neighboring organs. The cases of Kapsinow,[19] Peters and Milne,[1] Caussade, Surmont and Lacapère,[21] are representative of this mechanism.

The clinical picture of tumor of the heart is decidedly variable. There are no pathognomonic signs and the condition has never been diagnosed *intra vitam*. Krehl,[38] Fraenkel, Pavlowsky[40] and others have studied and laid stress on certain symptoms, but in the main they show little difference from the ordinary failing heart of myocardial insufficiency or the general failure as noted in the toxemia of widespread malignant disease. The location of metastases is of utmost importance. Tumors of the epicardium may produce hemorrhagic exudate into the pericardial cavity (Fraenkel) or cancer cells may be found in the sediment of such an exudate (Bosco). Tumors which encroach upon the chambers of the heart may produce swelling of the veins and anemia of the arteries (Pavlowsky). Pedunculated grafts or grafts lying free in the heart cavities may produce a ball-valve effect with change of posture. Tumors engrafted upon the endocardium or the valves (vegetative cancerous endocarditis), besides producing multiple emboli, can produce symptoms of valvular insufficiency and stenosis (Rist and Rolland, Widal and Abrami). Tumors disseminated throughout the cardiac muscle can modify the functional condition of the myocardium or, if rapidly growing, can

lead to disintegration of the cardiac mechanism and pathological change in the muscle fibers (Warthin). Anginal attacks have occurred (Ingram[39]), but it is questionable in this case whether the tumor nodules involved the patency of the coronary vessels. Involvement of the conduction mechanism may act as a cause for bradycardia with dissociation (Barthélémy). Roentgenograms may show a changed cardiac contour, if the tumor is large and obviously extends only in one direction, in a way that does not tally with any of the usual morbid states.

The cases reported below are five in number,—three of sarcoma and two of carcinoma. Of the three, one is sarcoma of the kidney; a second, lymphosarcoma of the mediastinal lymph glands, and the third, that of lymphosarcoma of the retroperitoneal lymph glands. The cases of carcinoma are of the bronchus and of the lung. All the cases showed, in addition to cardiac metastases, involvement of either the lungs, pleura, or mediastinal lymph glands. Furthermore, one is impressed with the latency of the cardiac lesions. These cases all resemble those of the average collected series, in that in no instance was a metastatic cardiac condition suspected during life.

REPORT OF CASES

CASE 1.—D. G., aged five years, male, Italian. About three months previously this child was operated upon for a condition which the attending physician diagnosed as acute appendicitis. The surgeon stated that a sarcoma of the ileum was found and the wound closed without further manipulation. About a month later the neck began to swell and breathing became difficult and noisy. The swelling remained stationary for about three weeks previous to admission at the Stanford Clinic in 1918. At that time the principal complaints were difficulty in breathing, cough, under-nutrition, loss of weight and strength.

The physical examination revealed a child undernourished and somewhat emaciated. His breathing was rapid and noisy. The thyroid was enormously enlarged and very hard, but not nodular. There were no positive eye signs of exophthalmic goiter. The chest showed retraction of the interspaces with each inspiration; no râles heard, and the percussion note and fremitus showed no abnormality. The heart was rapid and regular; no murmurs heard. The contour was not enlarged nor abnormal in outline; the apex impulse felt in the fourth intercostal space in midclavicular line. No friction rub was noted; pulses were synchronous and equal. The abdomen was irregularly pigmented, and moderately distended, with enlarged veins running upward from the region of the umbilicus. The liver edge was not felt; spleen was not felt. A hard, immovable, nontender tumor was easily palpable in the left lower quadrant in the region of the left kidney and extended downward just above the crest of the ileum. Reflexes equal. Death two weeks after admission.

Autopsy (Dr. Ophuls) *Anatomical Diagnosis.*—Sarcoma of kidney, round celled; sarcoma, metastatic, of lymph glands; sarcoma, metastatic, of heart; sarcoma, metastatic, of pericardium; sarcoma, metastatic, of intestine; sarcoma, metastatic, of thyroid; bronchial pneumonia. Heart: The pericardium contained an abnormal amount of turbid fluid. It showed a number of firm tumor nodules around the corona. The heart muscle was of normal thickness, but somewhat pale. The valves were normal. In the right auricle there was a large dense tumor mass involving

all that portion overlying the aorta. In the left ventricle on the septum, there was a tumor mass under the intima involving some of the muscular trabeculae. There was also a similar mass on the lateral wall of the right ventricle. Lungs: On the anterior margin of the lower lobe of the left lung, there was a small metastatic tumor. The right lung contained no nodules and the hilus glands were free. There was no tumor involvement anywhere in the pleura.

CASE 2.—P. H., male, aged fifty-seven years, Montenegrin. Patient entered San Francisco Hospital (Stanford Service) in February, 1919, with the complaint of cough, hoarseness, and a mass above the left clavicle. He denied venereal disease and except for an attack of malaria, at the age of fifty-five, had been in good health up to four or five months before, when he began to lose weight and feel weak. Simultaneously the patient began to cough, expectorated some blood, and experienced night sweats. Two months previous to entry he noticed a small bean-sized lump in the left supraclavicular region. About a month later a second lump was noted in the same region and both had since steadily increased in size.

Physical Examination.—The patient was emaciated and somewhat pale. Well marked supra- and infraclavicular muscle atrophy noted. Pupils reacted to light. The tonsils were not remarkable. In the posterior triangle of the neck and above the clavicle on the left side, were two oval masses, the posterior one being the larger and about the size of a golf ball. Around the edges of these were felt several smaller bean-sized masses, extending to the posterior chain in the neck. The masses were of about the consistency of hard rubber and were not attached to the skin or bound down to the deeper structures. The chest was symmetrical; expansion was equal; no venous stasis noted. Both apices were dull and the normal retromanubrial dullness was increased. Bronchovesicular breathing was heard at both tops with crepitant râles and many musical râles. It was difficult to percuss the cardiac area, the dullness of which merged with the retromanubrial dullness above noted. The heard rhythm was regular, rate not excessive, and no murmurs were noted in any of the valvular areas. Examination of the abdomen was essentially negative; extremities negative; reflexes present. The urine showed a moderate amount of pus and a slight trace of albumen. Sputum was negative for tubercle bacilli; blood Wassermann was negative. X-ray examination showed the mediastinal glands heavily infiltrated on both sides of the chest, especially on the right.

Death occurred thirteen months after admission.

Autopsy (Dr. Ophuls) *Anatomical Diagnosis.*—Tuberculosis of the lungs, chronic; tuberculosis of the bronchi; tuberculosis of intestines; tuberculosis of lymph glands, peribronchial, mesenteric; carcinoma of lung with metastases in lymph glands; carcinoma, metastatic, of myocardium.

Heart: In the pericardium was about 100 c.c. of clear fluid. Pericardium over the left auricle and upper part of left ventricle was studded with small, whitish tumor nodules from the size of a bird seed to 1.5 cm. in diameter. The tumor nodules had infiltrated the conus quite deeply. The heart was about three-quarters normal size. The muscles showed marked brown atrophy. The valves showed a few yellow spots on the left side. There were a few similar spots noted in the intima of the coronaries. There was a mass of tumor around the stem of the right coronary. The tumors of the pericardium also invaded the left ventricle. The glands of the mediastinum were very large and hard with large caseous areas. Lungs: In the upper lobe of the left lung posterior there was a large cavity of 6 cm. in diameter with trabeculated walls which was covered internally with an irregular layer of white tumor. One of the large branches of the left main bronchus opened into the cavity. The mucous membrane of this bronchus showed a rather superficial ulceration. In the upper right posterior lobe

was another cavity, 7 cm. in diameter, filled with cheesy material, the wall also trabeculated. There was no tumor in this cavity. The mucous membrane of the right bronchus was filled with numerous partly ulcerated tumor nodules. Part of the upper left lobe showed moist consolidation and some groups of small nodules near the cavity. The left lower lobe contained some small nodules. The same condition was in the middle lobe. The right lower lobe was filled with small nodules and was partly consolidated. The peribronchial glands were fairly large and contained a few white nodules.

CASE 3.—P. W. P., female, aged seventy-eight years, American. Patient entered Lane Hospital in January, 1924, with the complaint of pain and swelling of the left shoulder of four weeks' duration. The past history is of no importance save for an attack of typhoid fever as a girl and severe pneumonia in 1906. There has been, however, a steady loss of weight (50 pounds) in the last six years. The present illness started six weeks before admission with pain in the left shoulder and back of neck. The shoulder became swollen and red and the pain steadily increased, becoming very severe two weeks ago.

Physical Examination.—The patient was somewhat emaciated. Pupils reacted to light; hearing impaired in both ears. Those teeth that remained were in poor condition. Over the region of the left scapula there was a large carbuncle. The expansion of both lungs was limited. At the left base, dullness with increased tactile and vocal fremitus was noted and many fine and coarse râles were heard over this area. In the right lung many coarse and squeaking râles were heard but no areas of consolidation were noted. The area of cardiac dullness was increased, the apex impulse being seen and felt 3 cm. outside the midclavicular line in the sixth interspace. No thrill was felt; a soft systolic murmur was noted over the entire precordia and transmitted to the axilla and back. A light friction rub was heard in the fourth interspace immediately to the left of the sternum. The pulses were synchronous, equal; rhythm regular; rate not excessive and vessel walls not remarkable. Blood pressure 106/65. Abdomen was essentially negative, liver and spleen not felt and no masses noted in the abdomen. Extremities were negative; reflexes equal. A moderate anemia was present and the white count was elevated to 28,100 cells, with 87 per cent of polynuclear leucocytes. No tubercle bacilli found in the sputum on repeated examination; blood Wassermann negative. The x-ray report suggested lobar pneumonia of the left lower lobe or tuberculosis with a superadded pneumonia. Neoplasm of the lung was considered but the evidence was incomplete. Death three weeks after admission.

Autopsy (Dr. Ophuls) *Anatomical Diagnosis.*—Pneumonia, chronic, healed, of left lower lobe; pleurisy, healed; carcinoma, of bronchus; carcinoma, metastatic, of heart; carcinoma, metastatic, of pancreas; carcinoma, metastatic, of adrenals; carcinoma, metastatic, of kidneys; carcinoma, metastatic, of liver; tuberculosis of lungs, apical, healed; endocarditis, chronic.

Heart: There was about 50 c.c. of clear fluid in the pericardium. The heart was about normal size; the wall of the right ventricle and right auricle was rather thin and flabby. The mitral orifice was narrow, just admitting the thumb. There was marked calcification at the base of the orifice. The two flaps were practically normal. The aortic cusps were irregularly thickened, and very extensively calcified. The aortic orifice was somewhat narrowed. The right coronary artery was somewhat thickened, partly calcified. The lumen was wide. The left coronary artery showed a few yellow spots in the intima. Some calcareous plaques appeared just above the sinus of Valsalva; base of aorta otherwise normal. Left ventricle was firm, about 11 mm. thick. In the anterior wall of the left ventricle there was a tumor nodule about 1.5 cm. in diameter.

Lungs: The left lung was small. There was a rather large scar at the left apex extending 1.5 cm. into the lung tissue. In the scar were several small bronchiectatic cavities. The left upper lobe was fairly large, emphysematous. Lung tissue showed moderate edema. Left lower lobe was very small, made up of dense cicatricial tissue throughout. At the right apex there was a very much smaller scar than at the left apex with bronchiectasis. Right lung was large, markedly emphysematous. Posterior two-thirds of right upper lobe showed a diffuse dark red moist consolidation. Bronchi in right upper lobe were filled with pus. Middle lobe was not consolidated. At the base of the lung posteriorly was a rather soft, greyish, badly defined tumor nodule about 4.5 cm. in largest diameter. The tumor was not directly connected with any large bronchus but on section the tumor was found to surround and infiltrate diffusely the wall of a small bronchus.

CASE 4.—J. M., male, aged four years, Italian. Patient was admitted to the medical ward of the Lane Hospital in October, 1914. He complained of swelling of the face and neck and shortness of breath of six weeks' duration which followed an attack of influenza, although the patient had suffered some loss of weight and strength previous to his illness. Family and past history were essentially negative.

Physical examination showed a well-developed boy, not appearing sick. The superficial veins of the forehead, neck and upper chest stood out prominently. The left pupil was slightly larger than the right; both reacted to light. There were no eye signs of exophthalmic goiter. The superficial veins of the neck were prominent. On each side behind the lower third of the sternomastoid muscle was a swelling extending from the midline outward and upward to the level of the thyroid cartilage. The portion behind the muscles was hard and nodular and somewhat tender. This tumor was thought to be thyroid, the lobes being relatively much larger than the isthmus. The superficial veins over upper chest and shoulders were moderately distended, more marked on the right side. The distension was much increased on coughing. The percussion note was dull across the upper chest between the parasternal lines, the dull area being continuous with the cardiac dullness below. Breath sounds at both bases were normal; no râles or rubs heard. It was difficult to know whether or not the cardiac dullness was increased. The apex impulse was not seen or felt. The sounds were normal, no murmurs heard in any of the valvular areas; no friction rub was noted. Pulses equal, synchronous, rhythm regular, not rapid. Abdomen was negative throughout. Blood count showed a moderate anemia with little change in the differential formula; urine negative; blood Wassermann negative. Radiographic study confirmed the physical examination in that there was a marked wide shadow of the superior mediastinum. Death occurred five months after admission.

Anatomical Diagnosis of Chest Organs. (Incomplete autopsy) (Dr. Ophuls).—Lymphosarcoma of mediastinum lymph glands; lymphosarcoma, metastatic, of heart.

Heart: The heart showed a very irregular shape, due to the development of white, rather soft tumor nodules in the heart muscle on both sides. There were three or four such nodules. The largest one, about 3 cm. in diameter, was situated in the wall of the left ventricle. It extended from the pericardium to the endocardium and had a yellowish necrotic center.

Mediastinum and lungs: Anterior mediastinum was filled with very hard, greyish white tumor which was evidently very firmly attached to the posterior surface of sternum. The tumor surrounded the large blood vessels and caused a very marked compression of the veins. Laterally it extended into the adjoining part of the lungs and below it had involved the pericardium at the base of the heart. On the inner surface of the pericardium the tumor formed flat, slightly projecting, white nodules 0.5 to 1.5 cm. in diameter. Posteriorly the tumor surrounded the trachea and bronchi, infiltrated the peribronchial lymph glands and had involved the lungs

at the hilus. It did not involve the esophagus, but had caused considerable compression of it.

Note: The irregular shape of the heart as noted in the postmortem record was not suspected by x-ray or physical examination.

CASE 5.—H. L., male, aged twenty-seven years, Swedish. Patient entered Lane Hospital in September, 1917, complaining of loss of weight, loss of strength, swelling of legs and ankles. Patient had worked hard nearly all his life and had been particularly well and strong up to four months before entering hospital when his present illness started. At that time he noted severe intermittent pains in the right upper quadrant of the abdomen. These became progressively more severe and with the increase in the severity of the pains, vomiting ensued. Patient was operated on two months previous to admission because of gradual increasing jaundice, vomiting, and abdominal pain. The operation revealed a carcinoma of the head of the pancreas. The family history and past history are of little importance.

Physical Examination: Patient was moderately developed but somewhat emaciated and icteric throughout the body. There was generalized edema of face, legs, and feet, and the contour of the abdomen suggested the presence of ascitic fluid. The head and neck were not remarkable save for edema and icteric sclerae. The thorax was well formed. The lungs were resonant throughout save a slight impairment at both bases; no râles were heard; tactile and vocal fremitus normal. The heart was not increased in size, sounds were regular; there were no murmurs noted in any of the valvular areas. The rate was not excessive, the rhythm was regular and no friction rub was noted. Pulses equal and synchronous, vessel walls not remarkable, blood pressure 110/60. The abdomen was distended and signs of fluid were present. The liver was greatly enlarged, extending 5 cm. below the costal margin. It was not tender and the edge was smooth. In the upper left quadrant, a movable, nodular tumor mass was noted which was irregular in shape, not tender, and about the size of a pigeon's egg. Rectal examination was negative. Death occurred two months after admission.

Autopsy (Dr. Ophuls) *Anatomical Diagnosis.*—Lymphosarcoma of retroperitoneal lymph glands; lymphosarcoma, metastatic, of mediastinal lymph glands; lymphosarcoma, metastatic, of mesentery and peritoneum; lymphosarcoma, metastatic, of pericardium; obstruction of bile duct; jaundice, bronchopneumonia.

Heart: The pericardium over upper part of right ventricle contained a dense nodular mass about 1 cm. in diameter. On incision this mass was shown to be a tumor. The heart was about normal in size, muscle firm. Heart valves were all apparently normal. Coronaries were tortuous, walls somewhat thickened, otherwise normal.

Lungs and mediastinum: Left lung was covered with fibrinous adhesions posteriorly. Lower lobe somewhat congested. Cut surface covered with foamy exudate. Branches of bronchi contained reddish foamy exudate. There were no tumor nodules felt in the lung. The right lung was the same as the left. Small scar at both apices. Mediastinal lymph nodes were quite firmly infiltrated with tumor mass.

CONCLUSIONS

1. Malignant disease of the heart is rare; secondary involvement being relatively more frequent than primary.

2. Primary newgrowths originating in all the principal organs which commonly show malignant change have secondarily involved the heart.

3. The incidence of cardiac metastases is relatively much higher when the lung, pleura, or mediastinum is involved either by primary newgrowth or secondarily to neoplasm elsewhere.

4. Hemorrhagic pericardial exudate with tumor cells in the sediment offers a method of diagnosis in some cases of malignant disease of the epicardium and of the pericardium. Fluid of this type is often absent.

5. Signs and symptoms referable to the cardiovascular system are for the most part latent. In none of the cases herein reported was the true cardiac condition suspected.

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Erratum

In the article by Gold and Edwards, entitled "The Effects of Ouabain on the Heart in the Presence of Hypercalcemia," October issue, the heading of the fourth column of Table IV, page 48, should read: Fatal Dose of Ouabain in Percentage of Fatal Dose for Normal Animal.

Department of Reviews and Abstracts

Collective Review

PAROXYSMAL ACCELERATION OF THE HEART RATE*

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PAROXYSMAL acceleration of the heart in many respects still remains a medical enigma. During the last few years, however, important contributions have been made and numerous unusual examples of paroxysmal rapid heart action have been recorded in the medical literature. It seems appropriate, therefore, to attempt to correlate these observations in the hope of stimulating further study and investigation. Electrocardiography has made possible much closer study and analysis of cases and the identification and classification of types.

There is still considerable difference of opinion regarding the types of paroxysmal acceleration of the heart to be included under the generally accepted term paroxysmal tachycardia. To avoid this controversy and to justify a consideration of all the clinical forms of marked and sudden cardiac acceleration this review is introduced by the broad title, paroxysmal acceleration of the heart rate. The forms to be discussed are all characterized by the sudden inception of extremely rapid heart action, the paroxysm lasting for a variable period and terminating abruptly. The forms comprise paroxysmal auricular tachycardia, paroxysmal flutter with rapid ventricular rate, paroxysmal auricular fibrillation with rapid rate, paroxysmal nodal (auriculoventricular) tachycardia and ventricular tachycardia. Lewis[72] insists that paroxysmal tachycardia, in its strict sense, is but a series of extrasystoles. According to this postulate, paroxysmal tachycardia would comprise auricular, nodal (auriculoventricular), and ventricular tachycardia. Opinions[30] differ regarding the existence of paroxysmal tachycardia arising at the sinoauricular node (nomotopic tachycardia), but records are available exhibiting complexes indistinguishable from those in normal tracings. Caution is necessary, however, in asserting that because disorders do not conform to arbitrary classifications, their occurrence is not possible.

Auricular flutter and fibrillation have their origin in a mechanism apparently totally different from paroxysmal tachycardia. Lewis

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and his coworkers[73-77, 79, 80] have shown the origin of flutter in a circus movement and have demonstrated the close relationship that exists between flutter and fibrillation.

EXPERIMENTAL PRODUCTION

Paroxysmal acceleration of heart action has been produced experimentally in various ways. Clamping of the aorta with consequent sudden rise in ventricular pressure, has resulted in the sudden inception of rapid heart action.[45] The production of myocardial ischemia by sudden closure of the venous channels of the heart[125] or ligation of the coronary arteries[67, 119] has likewise resulted in sudden cardiac acceleration. Similar results have been produced by administration, intravenously and otherwise,of drugs, such as digitalis,[24, 84, 85] strophanthin,[112] chloroform,[63] nicotine,[101] adrenalin,[50] ether,[93] pituitary extract,[106] quinidine,[54] potassium[90] and barium salts,[111] and aconitine.[25] It is evident that many different agents and various factors may produce paroxysms of rapid heart action in animals and, for want of a clearer understanding, the underlying mechanism is still best expressed by the rather vague term, increased cardiac irritability.

THE ROLE OF THE EXTRINSIC CARDIAC NERVES

There have been numerous investigations regarding the influence of the vagus and the sympathetic nerves on disorders in cardiac mechanism. That vagal pressure results in the sudden arrest of a paroxysm of rapid heart action is well known. Lewis[72] agrees to the statement that abolition of vagal tone may provoke paroxysms of tachycardia but that the fundamental cause embodies other factors. A low-grade underlying toxemia is suggested, rendering the heart unusually susceptible to abnormal activity of the extrinsic nerves. Serious doubt regarding this assumption becomes evident in the observation of patients who have experienced attacks of paroxysmal tachycardia for thirty or forty years and even then present no evidence of organic disease. It is difficult to believe that a toxemia of such chronicity would not demonstrably affect the heart anatomically.

Bouveret[14] believed that excitation of the accelerator nerves, probably in the intracardiac ganglia, played an important part in the production of paroxysmal tachycardia. Owing to the normal findings during the intervals between attacks he concluded that the attacks were the result of disturbances of innervation. The frequent occurrence of paroxysms of rapid heart action in apparently normal hearts obviously renders the concept of neurogenic cause difficult to disprove. The frequent relationship of emotional disturbances to the onset of a paroxysm and the clear-cut incidence in many patients

with poor nervous stability strongly suggest that the manifestation is purely neurogenic in many cases.

Graber[41] recently published an interesting case of paroxysmal tachycardia in which the vagi were degenerated by pressure from the enlarged mediastinal lymph nodes of Hodgkin's disease.

THE EFFECT OF PAROXYSMAL ACCELERATION OF HEART RATE ON THE CIRCULATION

During the last few years the response of the coronary circulation to extreme acceleration of the heart has been studied on several occasions. Barcroft, Bock and Roughton[2] investigated the circulation of a patient during seizures of paroxysmal tachycardia. They observed lowering of the minute volume to nearly one-third its normal value and a decrease in the systolic output of the heart from 77.5 c.c. to 12.9 c.c. during the attack. They found no reduction in the degree of saturation of the arterial blood, but a rather high degree of saturation of the mixed venous blood, indicative, they believed, of retarded circulation.

The blood gases in a case of paroxysmal auricular tachycardia were studied by Carter and Stewart, who observed a marked decrease in the degree of arterial saturation, low oxygen saturation of the venous blood, and a greatly increased coefficient of utilization during the attack. These findings were interpreted as indicating a slow rate of circulation.

By producing regular tachycardia in dogs, Stewart and Crawford found that the blood flow was usually unchanged, but in one-third of their observations a reduction occurred, and about the same number of animals showed a decrease in the oxygen saturation of the arterial blood, ranging from 4 to 7 per cent.

Miller, Smith, and Graber in studying the effects of retardation and acceleration of heart rate on the coronary circulation, found a decrease and an increase in circulation within certain limits. The most striking changes were evident when relatively great changes in cardiac rate were induced. These authors[122] in a previous investigation showed that the maintenance of an efficient coronary circulation is fundamentally dependent on the height of the diastolic pressure and that changes in the systolic pressure influence the coronary circulation to a lesser degree.

These experimental studies agree quite well and show a slowing of circulation during some paroxysms of tachycardia. From a consideration of the remarkable adaptability of the cardiovascular mechanism, it is not difficult to realize that variations in the response of the circulation in different cases may occur. Great acceleration of cardiac rate maintained for a relatively long period would probably subject the rate of circulation to definite changes.

GENERAL CONSIDERATION OF PAROXYSMAL ACCELERATION OF THE HEART RATE

The cases in the present series were all characterized by paroxysms of rapid heart action with abrupt onset and sudden termination, the duration of the attacks being variable. There was a slightly greater incidence among males than among females, 59 per cent and 41 per cent respectively. Seventy-five per cent of the cases occurred in patients over the age of forty and 62 per cent in the fifth and sixth decades. There were no cases under the twentieth year. I have just observed a case of paroxysmal nodal (auriculoventricular) tachycardia in a boy aged six years who is not included in the series. The oldest patient was aged seventy-eight years.

The youngest patient in any case was an infant four days old mentioned in a report by Werley.[132] Other cases in infants have been described by Colgate and McCulloch[22] twenty-one and twenty-four days), Lewis[71] (three months), and Koplik (twenty-two months).

As a rule the paroxysms are of relatively short duration, lasting from a few minutes to several hours. Cases have, however, been reported in which the paroxysms lasted a remarkably long time and recovery occurred. Bernstein reported a case in which the paroxysm lasted fourteen and a half days and Porter one in which it lasted one hundred and fifty-three hours. In one case in the present series it lasted forty-two days, with recovery; the ventricular rate constantly hovered in the vicinity of 200.

The occurrence of attacks is variable, but in my experience it appears that the longer they have persisted, the more frequent are the repetitions. The attacks at first may occur only several times a year, and later may occur frequently in one day.

In about 40 per cent of the cases no demonstrable evidence of structural cardiac injury was elicited. In those cases in which organic cardiac disease was present the findings indicated many different types. The individual type most commonly represented was that associated with exophthalmic goiter.

The symptoms of the attacks are not constant, and seem to be determined by the severity and duration of the paroxysm and by the presence or absence of cardiac disease. Prostration, extremely rapid heart action, great anxiety, and shortness of breath are probably the most constant symptoms. The prostration may be slight or so marked that the patient exhibits all the signs of profound shock. The latter, in my experience, has occurred especially in those cases associated with a marked fall in blood pressure. Nausea and vomiting occasionally occur, and the latter is at times abruptly followed by cessation of the attack.

The face is often pallid and not infrequently a definite cyanotic tinge is present. In a number of instances, pulmonary edema with the expectoration of frothy, red-tinged material has been observed. The paroxysms have been severe in all these cases and of several hours' duration. This association has been observed in a case in which no organic cardiac disease could be demonstrated.

Some of the most interesting and at times alarming manifestations of paroxysms of tachycardia are those referable to the brain. Savini, and Esmein and Donzelot mentioned those phenomena, but the first comprehensive study was reported by Barnes. Fifteen cases formed the basis of his investigation. The mildest and most frequent symptom was vertigo, occurring in about half the cases. Next in frequency was temporary blindness, occurring in six cases. In five cases the patient fell during the attack but remained conscious; syncope occurred in four cases and epileptiform convulsions in two. In ten cases organic heart disease was not demonstrable. It is interesting to note that Barnes found these cerebral manifestations occurring most frequently when the origin of the cardiac impulse and its propagation deviated the furthest from normal. He attributes the manifestations to cerebral anemia and discusses the probable underlying physiological changes. The case reported by Thomas and Post is of interest in this discussion; paroxysms of tachycardia were invariably associated with migraine.

Another interesting group of cases is that in which the paroxysms are associated with cardiac pain. These cases have recently been studied by Barnes and Willius. In an analysis of 380 cases it was found that cardiac pain occurred in 5 per cent. The pain was similar in type and situation to that seen in angina pectoris. The pain differed from that of angina pectoris in that the factors that precipitate attacks of angina pectoris were absent and the painful seizures tended to be prolonged without having a serious outcome. In several of these cases a marked fall occurred in both systolic and diastolic blood pressure, undoubtedly producing a status comparable to that brought about experimentally by Smith and his coworkers.[122]

It is probable that the painful attacks occurring during the periods of rapid heart action result from deficient coronary circulation or from diminished oxygen saturation giving rise to myocardial anoxemia. Myocardial fatigue, the result of continued extreme acceleration of the heart, is in all probability a contributory factor.

In many cases environmental influences bear a definite relationship to the precipitation of the attack. The outstanding factors are excitement, exertion, and the ingestion of food. Abdominal flatulence, various emotional states and sudden changes in posture are other factors cited by patients.

Cases have been reported in which the patient has apparently had the power to arrest the attacks voluntarily. Such examples have been published by Carter and Wedd and by Fussell and Wolferth. Influences presumably calling the vagi into play, such as holding the breath, forced swallowing, vomiting, and so forth, have been recorded. In Carter and Wedd's case, however, vagal pressure repeatedly failed to interrupt the rapid rhythm.

TYPES OF PAROXYSMAL ACCELERATION OF THE HEART RATE

Paroxysmal Auricular Tachycardia.—Paroxysmal auricular tachycardia results from an ectopic focus of stimulus production at some point in the auricular musculature. Each auricular beat is succeeded by a ventricular beat, and the rate usually does not attain 200 a minute.

This form of paroxysmal heart acceleration occurs in the presence of cardiac disease as well as in cases in which disease is not demonstrable. Numerous clinical records of this disorder have been published.[1, 4, 19, 23, 32, 44, 57, 61, 66, 68, 89, 97, 109, 137]

Marvin and White have recorded an unusual case in which the paroxysms of auricular tachycardia were interrupted by ectopic beats arising in the ventricle without alteration of the dominant rhythm. Barker's[4] case also is unique; ventricular tachycardia occurred during an attack of paroxysmal auricular tachycardia.

Paroxysmal Auricular Flutter.—Many examples of paroxysmal auricular flutter have been recorded in medical literature.[3, 11, 42, 48, 51, 86, 88, 116, 120, 131, 135, 138, 141, 142, 145] Lewis and his coworkers[73-77, 79, 80] have explained flutter as the result of a circus movement following a central path in the auricle. The cases are separated into pure and impure flutter, depending on the degree of regularity of auricular deflections. The electrocardiograms are characterized by extremely rapid auricular waves exceeding 200 each minute. The acceleration of the auricles is at times extreme, a frequency of 375[51] and 390[138] beats each minute being attained.

In the present series, paroxysmal auricular flutter has been observed most frequently with exophthalmic goiter and with mitral stenosis, although its presence in other pathological states has been observed. I have never observed flutter when the heart has been free from disease. In most cases, varying degrees of auriculoventricular block exist although several instances of 1:1 conduction are recorded.[11, 88, 116, 135] I[138] reported an interesting and unusual case in which paroxysmal flutter and ventricular tachycardia coexisted.

Paroxysmal Auricular Fibrillation.—Rapid paroxysms of auricular fibrillation are not uncommon.[5, 9, 12, 26, 34, 35, 56, 58, 82, 100, 102, 105, 108, 123, 139, 140, 144] They not infrequently occur in cases of exophthalmic goiter and hyperfunctioning adenomatous goiter.[5, 9, 139, 140] Mitral stenosis, especially during the stage of failure, is likewise a condition frequently

associated with rapid paroxysmal auricular fibrillation. There are few varieties of heart disease that at some time are not subject to these paroxysms. Boas[12] even observed this condition in a case of marked scoliosis. It has been observed by Resnik[105] following treatment with digitalis.

The paroxysms are frequently transient but at times last hours and even days. Auricular fibrillation, in my experience, has never been encountered in the absence of evidence of heart disease. Falconer and Dean[31] and also Schwarzmann,[114] have observed auricular fibrillation as a temporary accompaniment of heart-block.

Paroxysmal Nodal (Auriculoventricular) Tachycardia.—Published examples of paroxysmal nodal (auriculoventricular) tachycardia are not frequent[27, 72, 99, 107, 137] although the records at the Mayo Clinic contain nearly fifty such cases.

Englemann was the first to show that the auriculoventricular node is endowed with the property of automatism following the application of the first Stannius ligature in the frog. The autonomic property of the auriculoventricular node is usually not in evidence owing to the greater rhythmicity of the sinus node. Excitation of the auriculoventricular node has been accomplished in various ways. Lewis,[70] and Meek and Eyster[92] were able to produce nodal rhythm by stimulation of the right vagus and Rothberger and Winterberg[111] by stimulation of the left accelerator.

Three types of paroxysmal nodal (auriculoventricular) tachycardia are recognized, depending presumably on the site of origin in the auriculoventricular node. When the P-R interval is reduced, it is believed that the ectopic focus is situated in the upper portion of the node. When the P-R interval is absent the rhythm presumably originates in the central portion of the node and when an R-P interval exists, the focus is believed to be in the lower portion of the node. Meakins has called attention to the fact that the P-wave is frequently inverted. Drury published an interesting case of paroxysmal tachycardia of nodal (auriculoventricular) origin in which retrograde heart-block and reciprocal rhythm occurred.

Paroxysmal Ventricular Tachycardia.—An increasing number of cases of paroxysmal ventricular tachycardia are being recorded.[4, 15, 20, 33, 37, 38, 40, 43, 46, 49, 62, 69, 89, 103, 104, 110, 115, 117, 127, 129, 136, 138, 145] It is apparently always the result of myocardial disease when it occurs independently of the action of drugs. Robinson and Herrmann, and Willius[136] have recorded instances in which necropsy has revealed obliterative processes of the left anterior descending coronary branch. It has been found to occur during the administration of digitalis[28, 83, 104, 115], strophanthin,[59] quinidine,[13, 21, 64, 65, 78, 96, 118] and chloroform and epinephrin.[81]

The electrocardiograms are successions of ectopic ventricular contractions and, with few exceptions, the complexes exhibit marked aberration. Auricles and ventricles usually contract at the same rate although, in Palfrey's case, the auricular rate exceeded that of the ventricles. Wolferth and McMillan, and Levine and Curtiss have published cases in which auricular fibrillation occurred during the paroxysms of ventricular tachycardia.

Barker[4] reported the combination of auricular and ventricular tachycardia and Willius,[138] auricular flutter and ventricular tachycardia.

Strong and Levine have called attention to the fact that the ventricular rate is usually irregular. Levine[60] has made an interesting observation in ventricular tachycardia that is helpful in the recognition of the disorder before graphic records are available. He has noted a variation in the intensity of the heart sounds at the apex, which apparently does not occur in the other forms of paroxysmal acceleration with the exception of auricular fibrillation, which would hardly be confused with the others.

Retrograde conduction in ventricular tachycardia has been described by Scott.[117]

PROGNOSIS

Barnes and Willius[7] in a study of 102 cases of paroxysmal acceleration of the heart rate concluded that the prognosis is largely determined by the type and degree of the associated cardiac disease. The higher death rates occurred in coronary and aortic disease, diseases that in themselves entail a relatively great mortality. Auricular flutter carried the highest death rate. McLester's conclusions regarding prognosis agree quite well with these.

TREATMENT

The treatment of paroxysms of rapid heart action, with the exception of auricular fibrillation and flutter, is still unsatisfactory. Occasionally, cases are encountered in which vagal pressure abruptly terminates the attack. This procedure should always be attempted. In exceptional instances the continued use of digitalis[61, 124] has been recommended but, in my experience, the results of this form of treatment have been very disappointing, except in auricular fibrillation and flutter. Here the intramuscular injection of digitalis often produces a definite effect within from three to four hours.[18]

Quinidine[47, 52, 55, 62, 95, 97, 121, 133, 134, 138] has probably given the most satisfactory results. Many cases are, however, refractory to its use. Singer and Winterberg advocate the intravenous administration of quinidine during the attacks. However, the oral administration in appropriate dosage over relatively long periods of time seems to be preferred.

The eradication of such causal influences as occur in exophthalmic goiter and in hyperfunctioning adenomatous goiter usually permanently abolishes the paroxysms of rapid heart action.

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Selected Abstracts

Dally, J. F. Halls: Prevention of Rheumatic Heart Disease in Children. Brit. Jour. Child. Dis., June, 1927, xxiv, 7.

The author points out the prevalence of rheumatic manifestations among English school children where between 15 per cent and 29 per cent suffer from one or more forms of rheumatism. Poynton's and Mackie's figures showing the frequency of cardiac involvement in rheumatic fever are quoted.

Recognition of mild rheumatic manifestations such as stiffness of muscles and a slight sore throat is not enough, as children showing these symptoms may already be victims of rheumatism. It must be remembered too, that children do not show the acute joint symptoms of adults. The condition is subacute or chronic and involves the nerves, and the muscles, including the heart.

The author stresses the importance of recognizing a rheumatic diathesis rather than assuming a specific bacterial infection. He notes the work of Llewellyn on endocrine imbalance in rheumatism.

It is necessary that life histories of potential rheumatic children should be studied along side those of rheumatic and controlled groups, over long periods. For this purpose, the author recommends the institution of Children's Cardiac Clinics, where the resistance of the patient can be built up along the lines of attack common in rheumatism, namely, the skin, the mucous membrane and the muscles.

Strickland-Goodall, M. B.: The Myocardium. Canadian Med. Assn. Jour., 1927, xvii, 881.

In this resumé of present day conceptions of heart muscle anatomy and physiology, the author points out the part played by the heart muscle in maintaining efficient circulation of the blood. He emphasizes in particular, the importance of the ventricular muscle. The efficiency of the right heart depends on adequate filling; myocardial integrity, especially of the pulmonary base; an efficient tricuspid tensing mechanism; systematic stimulation; and a free outlet.

An efficient left ventricle muscle depends on adequate filling; myocardial integrity of the aortic base; an efficient valve closure in normal supraventricular stimulus; and a free outlet.

Rozkowski, Ch.: Percussion of the Manubrium Sterni in Fusiform Dilatation of the Arch. of the Aorta. Arch. des Maladies du Coeur, May, 1927, p. 299.

The author shows that percussion of the manubrium sterni may be used to advantage in the diagnosis of dilatation of the arch of the aorta. In these cases alteration of the percussion note may be marked over the manubrium when percussion of the right border of the body of the sternum fails to show any change. The dullness may not be absolute though the sense of resistance is always increased. The author emphasizes that age and sex determine slight differences in the dullness and that in normal individuals variations may be due to the individual structure of the chest; the differing relation between the aorta and the posterior aspect of the sternum; lung condition; and the important factor of the position of the patient during the examination. The patient should be examined

in the sitting posture with the chest inclined forward at an angle of 45°. This position brings out clearly the aortic dullness compared with the pulmonary resonance. The author uses digital percussion and begins at the first left intercostal space, percusses the lower part of the manubrium and gradually moves toward the first right intercostal space. With this position and technic, alterations in the aortic width are easily made out. In normal subjects of both sexes and between twenty-five and forty-five years of age, the average transverse diameter was found to be for men 3.5 cm.; for women 3 cm. In a similar comparison of older subjects, many of whom had cardiovascular disease of mild degree or lung pathology, the average diameter for the men was 4 to 4.5 cm., for the women 3.5 to 4 cm. The third group who all showed an increase in transverse diameter between 4.5 and 7.5 cm., were all subjects of cardiorenal and vascular disease, and a syphilitic infection was present in many individuals in this third group. The author deduces from this that dilatation of the aorta is a presumptive sign of an old syphilitic infection.

Delhaye, A. and de Groodt, A.: Vegetative Endocarditis of the Tricuspid and Pulmonary Valves of a Child, the Subject of Congenital Heart Disease. Arch. des Maladies du Coeur, May, 1927, xx, 309.

The authors describe a case of infectious endocarditis, superimposed on a congenital cardiac malformation in a boy of sixteen years. The clinical diagnosis was that of pulmonary stenosis with a patent interventricular septum and generalized tuberculosis. Blood cultures were negative. The patient died after an afebrile illness of four months duration. Autopsy showed pulmonary stenosis with a vegetative endocarditis of the pulmonary and tricuspid valves and the presence of preagonal thrombi on the former. The authors note the absence during life of auscultatory signs of tricuspid disease. The right sided cardiac involvement which was present was considered to be due partly to the preexisting pulmonary stenosis, partly to the presence of thrombi in the pulmonary artery. Terminal edema which was present was explained as either due to the infection or else to failure of the right heart following the tricuspid insufficiency.

Taylor, Ruth E.: Influenzal Pericarditis. Jour. Am. Med. Assn., 1927, lxxxix, 347.

A case of pneumonia, pericarditis and laryngitis first received attention because of symptoms of laryngeal obstruction. The disease, which occurred when influenza was not epidemic, ran a rapid course. The influenza bacillus was isolated from the lungs and pericardial fluid in pure culture.

Postmortem examination revealed a pericardial cavity distended with pus and fibrin, which covered the visceral surface of the pericardium with a shaggy green gray coating. The myocardium was soft and flabby.

Hyman, Albert S.: Postinfluenzal Bradycardia. Arch. Int. Med., 1927, xl, 120.

The author observed the pulse rate and cardiac mechanism in patients recovering from influenza by means of electrocardiographic and polygraphic tracings.

Altogether in the study seventeen patients were included, six of which are used as illustrations in the paper. He describes three degrees of depression of the sinus node as the result of the toxin influence.

The first degree consists of the pulse rate of about 60 beats a minute when the previously noted rate has been from 74 to 88. The second degree of depression of the pacemaker mechanism produces a bradycardia of from 40 to 50 beats a minute with an irregularity which in many respects clinically suggests escaped nodal beats. Further depression apparently results in the escape of more such

beats to the extent that every other impulse may be so produced. The third degree of nodal depression is so extreme that the independent ventricular rhythm occurs with an irregularly slow pulse of from 28 to 38 beats a minute.

The clinical importance of detecting this condition cannot be overemphasized, for it may be readily confused at the bedside with partial and complete heart block associated with extrasystoles. While toxemic depression of the pacemaker mechanism is relatively innocuous and apparently leaves the heart undamaged, heart block of the second and third degrees following an acute infectious disease usually suggests extensive mischief suffered by the conducting system and perhaps irreparable myocardial injury.

Smith, G. G.: The Circulation in Prostatic Surgery. Jour. Am. Med. Assn., 1927, lxxxix, 925.

In a personal series of 150 prostatectomies there were sixteen deaths. Of these, six were due directly to cardiac failure, and in two more the cardiac condition was a contributory cause.

The condition of the myocardium and its arteries is the important factor in the behavior of the heart during and after prostatectomy.

In the selection of the time and method of operation and the type of anesthesia, the surgeon must attach even greater weight to the condition of the cardiovascular system than to the condition of the kidneys.

The surgeon must understand the essentials of cardiac physiology and therapy if he would give his patients who undergo prostatectomy the best chance to survive.

Clark, J. H.: Acute Cardiac Dilatation. Jour. Am. Med. Assn., 1927, lxxxix, 21.

The author reports deaths following the intravenous injection of dextrose and physiological saline solutions. He points out that intravenous therapy is not the innocuous procedure it is generally considered and that the necessity of carefully choosing patients, particularly when large amounts of fluid are to be given, should be emphasized. If the injection is given slowly and a careful watch is kept of the pulse and cardiac condition by frequent blood pressure determinations made during the injection, such fatalities should be preventable.

Willius, Frederick A., and Killins, Wendell A.: The Occurrence and Significance of Electrocardiograms of Low Voltage. Arch. Int. Med., 1927, xl, 332.

This study comprises 140 cases presenting electrocardiograms of low voltage. This in the authors' experience is an incidence of 0.3 per cent. All cases presenting associated abnormalities, such as auricular flutter, auricular fibrillation, incomplete bundle-branch block, significant T-wave negativity, complete heart block, partial heart block, delayed auriculoventricular conduction and the ectopic tachycardias, were excluded in this study. These associated observations in themselves are significant, and when considered in conjunction with records of low voltage, they are confusing, and obscure the true issue. The criterion for the selection of cases was a record in which the QRS deflection did not deviate more than 5 mm. in either direction from the base line in any of the three customary leads. All records were standard; that is, a string deflection of 1 cm. corresponding to 1 millivolt of current.

The cardiac mortality among the group with cardiac disease was 30 per cent, whereas the cardiac mortality in the group comprised of various diseases was 2 per cent.

From the data submitted here it is not justifiable to conclude that electrocardiograms of low voltage unassociated with other graphic abnormalities indicate serious myocardial disease or are of serious prognostic importance.

Burrage, Walter S., and White, Paul D.: Digitalis in Pneumonia. Am. Jour. Med. Sci., 1927, clxxiv, 260.

The question of the advisability of using digitalis as a therapeutic agent in the treatment of pneumonia lead the authors to examine a series of two hundred and twenty-one cases of lobar pneumonia treated in the adult medical wards of the Massachusetts General Hospital during the five years from January, 1921 through December, 1925.

Of the two hundred and twenty-one cases, one hundred and ten or 49.8 per cent received no digitalis. The mortality of this group was 16 per cent, while in the group of cases receiving digitalis, the mortality was 39.6 per cent, nearly two and one-half times as great.

The patients receiving digitalis were divided into those who were digitalized and those who were not. The digitalized patients showed a mortality only five-eighths as high as those who were given no digitalis medication whatever. Those receiving nondigitalizing doses showed a mortality three and one-half times as high as those without any digitalis. In this group, the digitalis was administered unsystematically, in many instances being used as the last resort in about one-half of the cases at a time when they were very seriously ill.

In the group here considered, among which the percentages of complications and danger list patients is very similar, the lowest percentage of mortality was found in those patients who were digitalized, and next in those who received no digitalis. The definitely higher mortality among those cases receiving nondigitalizing doses should discourage this type of administration. If the drug is to be used, full digitalization should be accomplished. It appears that the systematic administration of digitalis in digitalizing doses may have been of benefit in this series of cases. No untoward effects from a toxic action of digitalis in the present series of cases were observed. Larger series more carefully controlled than heretofore as to age, severity both of epidemic and individual illness, complications, and amount of digitalis given, must be assembled before conclusive evidence can be obtained as to the value of digitalis in pneumonia. The data presented here, as in the case of Stone's series, do suggest that digitalis is of value in pneumonia when given in sufficient dosage; the cases, however, are inadequate in number to prove the matter.

Book Reviews

L'Angine de Poitrine et L'Angine Abdominale.—By D. Daniélopolu. Masson et Cie, Paris, 1927, pp. 443.

Although the subject of angina pectoris has been considered in innumerable monographs and books, the importance of the condition, the fascination which it always has for the physician and the reputation Daniélopolu has built up by his studies cause one eagerly to turn the pages of his new book.

The book is a voluminous one; the pages themselves are of large size, having almost the dimensions of an atlas. The figures are unusually clear and the colored plates accurate and artistic. There are altogether 159 figures. Physiological experiments, the anatomy of the neck and chest, the pathological anatomy of the heart and aorta are magnificently illustrated.

The value of the book lies not so much in its systematic description of the various aspects of the disease as in the fact that in it one has a complete presentation of the author's own views, logically developed as the results of his own researches.

Angina pectoris is defined as a cardiac symptom occurring in the form of an attack, consisting of a peculiar and special kind of pain and of modifications in the fundamental properties of the heart muscle.

The author divided angina pectoris into the *pure* and the *complicated* forms, discarding terms like "true" and "false" angina pectoris. The pure or uncomplicated type is unaccompanied by respiratory phenomena. The other form, in addition to the usual symptoms, is characterized by dyspnea, or acute pulmonary edema. The pure type is further subdivided into those cases with organic lesions and those without. If the characteristics of angina pectoris are present by sign and symptom, as described in the definition, it is a true one, no matter whether it be on an organic basis or not. The mechanism of the two is the same; that is, an insufficient circulation of the blood to the myocardium. In the organic cases, it is usually due to coronary artery disease, whereas in the nonorganic, it depends upon an imbalance between the work of the heart and its nutrition.

Daniélopolu insists that the *history* of the patient is all important; i.e., "l'interrogatoire du malade." Indeed, the physical examination may be entirely negative. Often, however, a dilatation of the aorta or a hypertrophy of the left ventricle may be seen on the orthodiagram; a pulsus alternans or a tachycardia may be present; or a hy-

pertension may be found. The author lays great stress on the electrocardiogram as a diagnostic aid.

Angina pectoris, according to Daniélopolu, is a phenomenon of the myocardium produced by insufficient blood supply of the muscle and launched by a group of cardiovascular reflexes. The heart itself presents certain vascular and nervous lesions which play a predisposing rôle, but the attack is precipitated by intermediary centripetal and centrifugal cardiovascular impulses. In great detail and with many illustrations, the anatomy and physiology of the sensory cardio-aortic nerve filaments are described; so, too, are the normal and pathological physiology of the blood supply of the heart muscle and the anatomy of the heart and aorta, as seen in individuals with angina pectoris. One is immediately struck by the great number of variations in nerve structure from individual to individual and one must conclude with Daniélopolu that only a surgeon who has become experienced in this work can hope for any success in operations upon these patients.

The author declares that in the posterior ganglia of the spinal cord there occurs the union of visceral sensory fibers with those of general cutaneous sensation. The eighth cervical and the first four dorsal spinal ganglia play a similar rôle for sensory fibers from the heart and aorta. The accelerator and the vagus nerves, the vasoconstrictor and the vasodilator centers of the bulb and upper spinal cord are similarly connected with sensory cardio-aortic fibers. Pressor and depressor fibers also lead to the spinal cord. Sensory cardio-aortic fibers enter into connection with vasomotor centers of the arm, particularly the left arm; these fibers probably connect with coronary vasomotor centers and hence reflexly from the heart and aorta the coronary supply can be influenced. Cardio-aortic sensory fibers are connected to centers of tonic voluntary muscle for the breast and arm, and with clonic muscle centers also.

In the normal state, the function of the heart is automatic and the sensory cardio-aortic fibers carry only vegetative reflexes. In pathological cases the heart may give rise to conscious sensations of pain, palpitation, angina, etc. In man there is, he believes, no anatomically distinct depressor nerve, such as is found in the rabbit, but the depressor effects, that is, the fall of blood pressure and slowing of the heart rate, are obtained through a series of nervous impulses from the heart and aorta which travel in the sympathetic trunk and in the vagus. The vertebral nerve is important, for stimulation of its central end in animals increases the output of the left ventricle, increases blood pressure, produces evidences of pain, etc.

The heart and aorta give rise not only to centrally directed depressor effects but to pressor changes as well. Excitation of these

fibers reflexly produces modifications in the blood pressure and heart rate, which effects are explained through connections these nerves make with the centers of vasoconstriction, vasodilatation, cardiac acceleration and retardation. Daniélopolu does not accept Mackenzie's idea of a visceromotor reflex to explain the contracture of the abdominal wall in appendicitis or the pectoral muscles in angina pectoris. Whereas, Mackenzie considers it a visceromotor action through connection with the cerebrospinal system, Daniélopolu considers it a visceromyotonic effect through the vegetative system which has a subconscious effect of tonic and clonic contracture of the muscle.

Besides the anastomotic circulation as a means of assuring myocardial blood supply, there is a direct circulation of the veins of Thebesius in the right auricle. Cases have been described in which the two coronaries have been found totally occluded; so in every such case the heart muscle must have depended solely on the Thebesian veins. Hence, in chronic coronary artery cases, circulation of the heart is assured, first, by anastomoses of these vessels and, secondly, by the veins of Thebesius. The latter supply may account for cases of hearts with closed coronaries which nevertheless gave rise to no attacks of angina pectoris during life.

The author discusses at length the four principal hypotheses concerning the pathogenesis of angina pectoris,—the aortalgia of Allbutt, neuralgia of the cardiac plexus, the myocardial insufficiency theory of Mackenzie, and the coronary artery disease theory of Hunter and Jenner,—and gives his reasons for rejecting each of these as a wholly satisfactory explanation.

His own hypothesis of the pathogenesis of angina pectoris is that of *fatigue* of the myocardium and the presence of a *pressor reflex.* According to the author, who first published his theory in 1916, the attack of angina pectoris is a phenomenon of fatigue of the myocardium, resembling fatigue of voluntary muscle. This is the result of an insufficiency of the blood supply of the heart, an event directly connected with the pressor reflex. Fatigue of *voluntary* muscle, the author states, is caused by an imbalance between the work performed and the blood supply, which leads to an intoxication of the muscle, and this in turn provokes paralysis and pain. *Myocardial* fatigue is a result of the imbalance between the work of the heart and its blood supply.

Other authors have explained angina pectoris as the result of insufficient blood supply of the heart for the work performed but, without exception, they have considered this insufficiency to be due to coronary artery disease solely. Daniélopolu adds the veins of Thebesius as a source of blood supply; hence, his theory explains the occurrence of grave coronary artery disease without angina pectoris.

The *predisposing factors* which provoke insufficient blood supply of the heart are chiefly coronary inflammation or atheroma and aortic lesions producing an obstruction around the coronary orifices. Abnormal reflexes may provoke a general vasoconstriction and more particularly a coronary vasoconstriction. Lesions of the cardiac and peri-aortic plexuses are predisposing factors which provoke insufficient blood supply of the heart; so, too, is a general hyperexcitability of the vegetative nervous system and of the visceral sensory system which predisposes to the different cardiovascular reflexes necessary to set off an attack.

The *determining factors* which provoke an attack are factors which augment the work of the heart, or which diminish still further its blood supply. For example, in a physical effort the arterial tension is increased, the heart accelerated and a strain put on the coronary circulation. The toxins produced in contraction are not destroyed and soon poison the muscle and produce fatigue. This explains, too, why paroxysmal tachycardias are occasionally accompanied by attacks of pain. An explanation, however, is required for the fact that an attack persists long after the exciting factor has disappeared. To explain this Daniélopolu uses his *pressor circle reflex.* Toxic substances of fatigue excite the nerve endings in the myocardium and so give rise to a series of cardio-aortic sensory reflexes in the vegetative nervous system. The heart accelerates, the blood pressure rises, and an intense vasoconstriction of the arm, with increased vasomotor oscillations, occurs and a hypertonicity of the pectoral and intercostal muscles follows.

Turning to the subject of treatment, it is found that the author discusses only briefly the medical aspects of this. His real contribution lies in the surgical treatment of the disease. He believes it is necessary to destroy the centripetal fibers that make up part of the vegetative reflexes; in other words, his method is to suppress the *pressor reflex.* The vagus, together with the inferior cervical and first dorsal ganglia, although they contain pathways for this reflex, are too important to destroy. One should section the nerves containing the sensory cardio-aortic fibers, but not those containing the centrifugal cardiac nerves.

Hence, in February, 1925, Daniélopolu proposed resection of the cervical sympathetic cord without touching the inferior cervical ganglion, sectioning branches of the cervical vagus which enter the thorax, cutting the vertebral nerve, sectioning the rami communicantes which unite the inferior cervical ganglion with that of the first thoracic and the sixth, seventh, and eighth cervicals, and finally sectioning of the nerve (when it exists) that leaves the superior laryngeal nerve to unite with the vagus. Whether or not the entire pro-

cedure is carried out depends on the severity of the pain and on the ability of the patient to stand the operation. Otherwise, section of the sympathetic cord without separation from the inferior cervical ganglion is performed only, or the vertebral nerve alone is cut with, or without, sectioning of the rami communicantes.

Any criticism of the work should begin with a commendation upon the clarity and logic that the author has applied to his task. He writes so persuasively that it is difficult at first to question his conclusions. The book is a compilation of his previous researches, a physiological interpretation of a clinical entity, or better still, a pathological-physiological treatise. Although it is highly desirable to explain disease symptoms on a physiological basis, it is exceedingly difficult in this field to apply to man results obtained from experiments performed on animals. Only thirteen case histories are cited in the entire book.

The subject is still obscure, and one should be wary of dogmatic statements. It must not be forgotten that the ideas of Daniélopolu are theories rather than proved facts.

In giving his rather brief medical treatment, the author insists that the nitrites and digitalis are most important. In this country his praise of digitalis and his faith in this drug as a cure or as symptomatic treatment will find criticism in many quarters. Most clinicians are doubtful of any benefit from this drug in cases of angina pectoris without myocardial failure, and some are convinced that it is contraindicated in acute cardiac infarction.

The matter of myocardial infarction brings up the point that nowhere in his book does the author distinguish clearly between angina pectoris of effort and the angina pectoris of coronary artery thrombosis. In his discussion of the symptomatology and treatment, he fails to utilize this very important distinction and so throughout the entire book one often feels uncertain as to which cases reference is made.

There will be general agreement with the author as to the importance of a careful history of the patient, but many will be surprised at his statement that significant changes in the electrocardiogram are always to be found during an attack of angina pectoris. That may possibly be true for those cases of anginal pain which mark the occurrence of an acute coronary occlusion, but it can hardly be asserted for all cases of the angina of effort.

In regard to Daniélopolu's operation, which after all is one of his main contributions to the subject of angina pectoris, his emphasis upon the importance of leaving the inferior cervical and the first dorsal ganglia intact will receive general approval.

The case reports of patients operated upon by the method of the author are very promising, but they are still too few and the time is

short for a final judgment. Only a much greater number of cases and a longer interval of time can decide the value of his particular operative procedure.

It is to be regretted that he lays down no rules for the selection of patients for the operation, as has recently been done, for example, by Levine and Newton. No discrimination is made between old and young, or between those with severe myocardial degeneration, who will, in any event, live only for a short while, and those whose myocardium is presumably good.

A. M. M.